=> index bioscience medicine

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS, CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 11:24:07 ON 31 JAN 2006

=> s ((phosphatidic(s)acid adj phosphatase) or (acid adj phosphatidyl (s) phosphatase) or (phosphatic adj acid (s) hydrolase) or (lipid (s) protein (s) phosphatase) or (phosphatidate (s) phosphatase))
3 FILE ADISCTI
4 FILE ADISINSIGHT
1 FILE ADISNEWS
77 FILE AGRICOLA
8 FILE ANABSTR
4 FILE AQUALINE
47 FILE AQUASCI
27 FILE BIOENG
545 FILE BIOSIS
85 FILE BIOTECHABS
85 FILE BIOTECHDS
524 FILE BIOTECHNO
265 FILE CABA
580 FILE CAPLUS
2 FILE CEABA-VTB
9 FILE CONFSCI
1 FILE CROPB
5 FILE CROPU
52 FILE DDFB
81 FILE DDFU
963 FILE DGENE
66 FILE DISSABS
52 FILE DRUGB
136 FILE DRUGU
19 FILE EMBAL
666 FILE EMBASE
578 FILE ESBIOBASE
82* FILE FEDRIP
8 FILE FROSTI
28 FILE FSTA
436 FILE GENBANK
94 FILE IFIPAT
2 FILE IMSDRUGNEWS
2 FILE IMSRESEARCH
46 FILE JICST-EPLUS
2 FILE KOSMET
361 FILE LIFESCI
639 FILE MEDLINE
29 FILE NIOSHTIC
9 FILE NTIS
16 FILE OCEAN
372 FILE PASCAL
10 FILE PROMT
18 FILE PROUSDDR
285 FILE SCISEARCH
279 FILE TOXCENTER
768 FILE USPATFULL
61 FILE USPAT2
7 FILE VETB
7 FILE VETU
9 FILE WATER
137 FILE WPIDS
1 FILE WPIFV
137 FILE WPINDEX
3 FILE IPA
5 FILE NLDB

L3 QUE ((PHOSPHATIDIC(S) ACID ADJ PHOSPHATASE) OR (ACID ADJ PHOSPHATIDYL (S)

PHOSPHATASE) OR (PHOSPHATIC ADJ ACID (S) HYDROLASE) OR (LIPID (S) PROT
EIN (S) PHOSPHATASE) OR (PHOSPHATIDATE (S) PHOSPHATASE))

=> d rank
F1 963 DGENE
F2 768 USPATFULL
F3 666 EMBASE
F4 639 MEDLINE
F5 580 CAPLUS
F6 578 ESBIOBASE
F7 545 BIOSIS
F8 524 BIOTECHNO
F9 436 GENBANK
F10 372 PASCAL
F11 361 LIFESCI
F12 285 SCISEARCH
F13 279 TOXCENTER
F14 265 CABA
F15 137 WPIDS
F16 137 WPINDEX
F17 136 DRUGU
F18 94 IFIPAT
F19 85 BIOTECHABS
F20 85 BIOTECHDS
F21 82* FEDRIP
F22 81 DDFU
F23 77 AGRICOLA

=> file f2-f8, f10-f15, f18, f19, f23

FILE 'USPATFULL' ENTERED AT 11:40:54 ON 31 JAN 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 11:40:54 ON 31 JAN 2006
Copyright (c) 2006 Elsevier B.V. All rights reserved.

FILE 'MEDLINE' ENTERED AT 11:40:54 ON 31 JAN 2006

FILE 'CAPLUS' ENTERED AT 11:40:54 ON 31 JAN 2006

COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'ESBIOBASE' ENTERED AT 11:40:54 ON 31 JAN 2006
COPYRIGHT (C) 2006 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'BIOSIS' ENTERED AT 11:40:54 ON 31 JAN 2006
Copyright (c) 2006 The Thomson Corporation

FILE 'BIOTECHNO' ENTERED AT 11:40:54 ON 31 JAN 2006
COPYRIGHT (C) 2006 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'PASCAL' ENTERED AT 11:40:54 ON 31 JAN 2006
COPYRIGHT (C) 2006 INIST-CNRS. All rights reserved.

FILE 'LIFESCI' ENTERED AT 11:40:54 ON 31 JAN 2006
COPYRIGHT (C) 2006 Cambridge Scientific Abstracts (CSA)

FILE 'SCISEARCH' ENTERED AT 11:40:54 ON 31 JAN 2006
Copyright (c) 2006 The Thomson Corporation

FILE 'TOXCENTER' ENTERED AT 11:40:54 ON 31 JAN 2006
COPYRIGHT (C) 2006 ACS

FILE 'CABA' ENTERED AT 11:40:54 ON 31 JAN 2006
COPYRIGHT (C) 2006 CAB INTERNATIONAL (CABI)

FILE 'WPIDS' ENTERED AT 11:40:54 ON 31 JAN 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE 'IFIPAT' ENTERED AT 11:40:54 ON 31 JAN 2006

COPYRIGHT (C) 2006 IFI CLAIMS(R) Patent Services (IFI)

FILE 'BIOTECHABS' ACCESS NOT AUTHORIZED

FILE 'AGRICOLA' ENTERED AT 11:40:54 ON 31 JAN 2006

=> s L3
10 FILES SEARCHED...
L4 6170 L3

=> s (gene or sequence or polynucleotide or recombinant or clone)(s)L4
7 FILES SEARCHED...
L5 1171 (GENE OR SEQUENCE OR POLYNUCLEOTIDE OR RECOMBINANT OR CLONE)(S)
L4

=> s (phosphatase or hydrolase)(s)L5
L6 1171 (PHOSPHATASE OR HYDROLASE)(S) L5

=> s phosphatase(s)L6
L7 1171 PHOSPHATASE(S) L6

=> s neutro?(s)L7
L8 21 NEUTRO?(S) L7

=> s neuro?(s)L7
5 FILES SEARCHED...
8 FILES SEARCHED...
L9 137 NEURO?(S) L7

=> s treat?(s)L9
8 FILES SEARCHED...
L10 21 TREAT?(S) L9

=> dup rem l9
PROCESSING COMPLETED FOR L9
L11 118 DUP REM L9 (19 DUPLICATES REMOVED)

=> dup rem l10
PROCESSING COMPLETED FOR L10
L12 20 DUP REM L10 (1 DUPLICATE REMOVED)

=> d ibib abs l12 1-20

L12 ANSWER 1 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2006:10654 USPATFULL
TITLE: LPA receptor agonists and antagonists and methods of use
INVENTOR(S): Miller, Duane D., Germantown, TN, UNITED STATES
Tigyi, Gabor, Memphis, TN, UNITED STATES
Durgam, Gangadhar G., Memphis, TN, UNITED STATES
Virag, Tamas, Chicago, IL, UNITED STATES
Walker, Michelle D., Memphis, TN, UNITED STATES
Tsukahara, Ryoko, Memphis, TN, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2006009507	A1	20060112
APPLICATION INFO.:	US 2004-963085	A1	20041012 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-509971P	20031009 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Edwin V. Merkel, Nixon Peabody LLP, Clinton Square, P.O. Box 31051, Rochester, NY, 14603-1051, US
NUMBER OF CLAIMS: 55
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 2768

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to compounds according to formula (I) as disclosed herein as well as pharmaceutical compositions which include those compounds. Also disclosed are methods of using such compounds, which have activity as agonists or as antagonists of LPA receptors; such methods including inhibiting LPA activity on an LPA receptor, modulating LPA receptor activity, treating cancer, enhancing cell proliferation, treating a wound, treating apoptosis or preserving or restoring function in a cell, tissue, or organ, culturing cells, preserving organ or tissue function, and treating a dermatological condition.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 2 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2006:3467 USPATFULL
TITLE: Method for preventing or treating obesity by modulating the activities of the pentose phosphate patway
INVENTOR(S): Xu, Zhengping, Gaithersburg, MD, UNITED STATES
PATENT ASSIGNEE(S): Minkon Biotechnology, Inc., Gaithersburg, MD, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2006002922	A1	20060105
APPLICATION INFO.:	US 2005-169944	A1	20050630 (11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2004-583617P	20040630 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: CROWELL & MORING LLP, INTELLECTUAL PROPERTY GROUP, P.O. BOX 14300, WASHINGTON, DC, 20044-4300, US
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 1080
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Method for preventing or treating overweight or obesity, the method comprising administering to a patient in need thereof an antagonist that inhibits gene expression or activity of an enzyme that is involved or related to the pentose phosphate pathway. Preferably, the enzyme is a transketolase, and the antagonist is an antibody, an antisense molecule, an siRNA molecule, a molecule for forming a triplex nucleic acid molecule with the enzyme-encoding polynucleotide. Also disclosed are pharmaceutical compositions comprising the same, and method for screening a substance that inhibits gene expression of a PPP enzyme or its function.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 3 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2005:299583 USPATFULL
TITLE: LPA receptor agonists and antagonists and methods of use
INVENTOR(S): Miller, Duane D., Germantown, TN, UNITED STATES
Tigyi, Gabor, Memphis, TN, UNITED STATES
Dalton, James T., Columbus, OH, UNITED STATES
Sardar, Vineet M., Cordova, TN, UNITED STATES
Elrod, Don B., College Station, TX, UNITED STATES
Xu, Huiping, Memphis, TN, UNITED STATES
Baker, Daniel L., Memphis, TN, UNITED STATES
Wang, Dean, Memphis, TN, UNITED STATES
Liliom, Karoly, Budapest, HUNGARY
Fischer, David J., Plymouth, MA, UNITED STATES
Virag, Tamas, Memphis, TN, UNITED STATES
Nusser, Nora, Memphis, TN, UNITED STATES

	NUMBER	KIND	DATE

PATENT INFORMATION: US 2005261252 A1 20051124
APPLICATION INFO.: US 2005-67884 A1 20050228 (11)
RELATED APPLN. INFO.: Division of Ser. No. US 2001-811838, filed on 19 Mar 2001, GRANTED, Pat. No. US 6875757

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-190370P	20000317 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Edwin V. Merkel, Nixon Peabody LLP, Clinton Square, P.O. Box 31051, Rochester, NY, 14603-1051, US
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 26 Drawing Page(s)
LINE COUNT: 4436
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compounds according to formula (I) as disclosed herein as well as pharmaceutical compositions which include those compounds. Also disclosed are methods of using such compounds, which have activity as agonists or as antagonists of LPA receptors; such methods including inhibiting LPA activity on an LPA receptor, modulating LPA receptor activity, treating cancer, enhancing cell proliferation, and treating a wound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 4 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2005:292912 USPATFULL
TITLE: Drug discovery assays based on the biology of chronic disease
INVENTOR(S): Polansky, Hanan, Rochester, NY, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005255458	A1	20051117
APPLICATION INFO.:	US 2003-611217	A1	20030701 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2002-223050, filed on 14 Aug 2002, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Hanan Polansky, 3159 S. Winton Rd., Rochester, NY, 14623, US
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 69 Drawing Page(s)
LINE COUNT: 23390
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Using the recently discovered biology of chronic disease, the invention presents new methods for evaluating the effectiveness of a compound for use in modulating the progression of chronic disease, for determining whether a subject has a chronic disease, or has an increased risk of developing clinical symptoms associated with such disease, and for treating chronic disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 5 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2005:183978 USPATFULL
TITLE: Novel polypeptides, and nucleic acids encoding the same
INVENTOR(S): Pennica, Diane, Burlingame, CA, UNITED STATES
Rastelli, Luca, Guilford, CT, UNITED STATES
PATENT ASSIGNEE(S): CuraGen Corporation, New Haven, CT, UNITED STATES (U.S. corporation)
Genentech, Inc., South San Francisco, CA, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005159373	A1	20050721

APPLICATION INFO.: US 2003-422335 A1 20030424 (10)
RELATED APPLN. INFO.: Division of Ser. No. US 2001-815248, filed on 22 Mar 2001, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-191258P	20000322 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN, 55402-0903, US
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1-32
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 4374
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An isolated polypeptide comprising an amino acid sequence having at least 80% sequence identity to the sequence SEQ ID NOS:2, 4, 6 or 8, polynucleotides encoding these peptides, and antibodies to the polypeptides are useful in treating cancers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 6 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2005:99636 USPATFULL
TITLE: Composition, synthesis and therapeutic applications of polyamines
INVENTOR(S): Murphy, Michael A, La Jolla, CA, UNITED STATES
Malachowski, Mitchell R, San Diego, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005085555	A1	20050421
APPLICATION INFO.:	US 2003-499931	A1	20021218 (10)
	WO 2002-US40732		20021218

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-17235, filed on 18 Dec 2001, PENDING Continuation-in-part of Ser. No. US 2003-486310, filed on 23 Feb 2000, GRANTED, Pat. No. US 6576672 A 371 of International Ser. No. WO 2003-US9817301, filed on 21 Aug 1998 Continuation of Ser. No. US 2003-915660, filed on 21 Aug 1997, GRANTED, Pat. No. US 5906996
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: CHARMASSON & BUCHACA & LEACH LLP, 1545 HOTEL CIRCLE SOUTH, SUITE 150, SAN DIEGO, CA, 92108-3412, US
NUMBER OF CLAIMS: 145
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 38 Drawing Page(s)
LINE COUNT: 5855
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to a process of synthesis and composition of open chain (ring), closed ring, linear branched and or substituted polyamines, polyamine derived tyrosine phosphatase inhibitors and PPAR partial agonists/partial antagonists via a series of substitution reactions and optimizing the bioavailability and biological activities of the compounds. Polyamines prevent the toxicty of neutoxins and diabetogenic toxins including paraquat, methyphenyl pyridine radical, rotenone, diazoxide, streptozotocin and alloxan. These polyamines can be to treat neurological, cardiovascular, endocrine acquired and inherited mitochondrial DNA damage diseases and other disorders in mammalian subjects, and more specifically to the therapy of Parkinson's disease, Alzheimer's disease, Lou Gehrig's disease, Binswanger's disease, Olivopontine Cerebellar Degeneration, Lewy Body disease, Diabetes, Stroke, Atherosclerosis, Myocardial Ischemia, Cardiomyopathy, Nephropathy, Ischemia, Glaucoma, Presbycussis, Cancer, Osteoporosis, Rheumatoid Arthritis, Inflammatory Bowel Disease, Multiple Sclerosis and as Antidotes to Toxin Exposure.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 7 OF 20 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-479336 [48] WPIDS
DOC. NO. CPI: C2005-145973
TITLE: (Down)regulating translational activity of a target gene in a nerve cell of the central nervous system, for treating, e.g. obstructive sleep apnea, by delivering a small interfering RNA composition to a target site.
DERWENT CLASS: B04 D16
INVENTOR(S): BAKER-HERMAN, T L; MITCHELL, G S
PATENT ASSIGNEE(S): (BAKE-I) BAKER-HERMAN T L; (MITC-I) MITCHELL G S; (WISC) WISCONSIN ALUMNI RES FOUND
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005059135	A2	20050630	(200548)*	EN	62
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2005234000	A1	20051020	(200569)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005059135	A2	WO 2004-US41339	20041210
US 2005234000	A1 Provisional	US 2003-529326P	20031212
		US 2004-9797	20041210

PRIORITY APPLN. INFO: US 2003-529326P 20031212; US 2004-9797 20041210
AN 2005-479336 [48] WPIDS
AB WO2005059135 A UPAB: 20050728
NOVELTY - (Down)regulating translational activity of a target gene in a nerve cell of the central nervous system of a mammal comprising delivering a small interfering RNA (siRNA) composition to a target site, e.g. muscle tissue on the mammal to cause downregulation of the target gene in the nerve cell, is new.

DETAILED DESCRIPTION - (Down)regulating translational activity of a target gene in a nerve cell of the central nervous system of a mammal comprises providing a small interfering RNA (siRNA) composition constructed to have a strand complementary to a portion of the target gene; and delivering the siRNA composition to a target site on the mammal to cause downregulation of the target gene in the nerve cell, where the target site is a muscle tissue innervated by nerve cell(s) or cerebrospinal space.

An INDEPENDENT CLAIM is also included for a kit for down regulating a target gene in a nerve cell in the central nervous system of a mammal, the kit comprising: (a) an siRNA composition constructed to have a strand complementary to a portion of the target gene; and (b) instructions for delivering the siRNA composition into a target site on the mammal, such that the target gene in the nerve cell is down-regulated.

ACTIVITY - CNS-Gen.; Respiratory-Gen. No biological data given.

MECHANISM OF ACTION - RNA Interference. No biological data given.

USE - The method is useful for treating a respiratory control disorder selected from obstructive sleep apnea, respiratory insufficiency following spinal cord injury, respiratory insufficiency caused by neurodegenerative motoneuron disease, respiratory deficiency due to polio and sudden infant death syndrome.

Dwg.0/13

L12 ANSWER 8 OF 20 IFIPAT COPYRIGHT 2006 IFI on STN

AN 10885284 IFIPAT;IFIUDB;IFICDB
TITLE: METHODS OF ISOLATION, EXPANSION AND DIFFERENTIATION OF FETAL STEM CELLS FROM CHORIONIC VILLUS, AMNIOTIC FLUID, AND PLACENTA AND THERAPEUTIC USES THEREOF
INVENTOR(S): Atala; Anthony, Winston Salem, NC, US
De Coppi; Paolo, Treviso, IT
PATENT ASSIGNEE(S): Unassigned
AGENT: DAVID S. RESNICK, 100 SUMMER STREET, NIXON PEABODY LLP, BOSTON, MA, 02110-2131, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2005124003	A1	20050609
APPLICATION INFORMATION:	US 2002-495419		20021115
	WO 2002-US36966		20021115
			20021115 PCT 371 date
			20021115 PCT 102(e) date

	NUMBER	DATE
PRIORITY APPLN. INFO.:	US 2001-335878P	20011115 (Provisional)
	US 2002-356295P	20020213 (Provisional)
FAMILY INFORMATION:	US 2005124003	20050609

DOCUMENT TYPE: Utility
Patent Application - First Publication
FILE SEGMENT: CHEMICAL
APPLICATION

NUMBER OF CLAIMS: 46 6 Figure(s).
DESCRIPTION OF FIGURES:
FIGS. 1A-1G show results from chorionic villi and amniotic cell characterization experiments. Between 0.8 and 3% of the amniotic and chorionic villi cells were c-kitpos (1A). The ckitpos cells did not stain with mouse stage specific embryonic antigen 1 (1B), but stained positively for human stage specific embryonic antigens 3 and 4 (1C and 1D). Analyses of late passage c-kitpos cells (PD 200) showed a normal karyotype (1E). Telomerase activity was evaluated using the Telomerase Repeat Amplification Protocol (TRAP) assay (1F). The chorionic villi and amniotic c-kitpos cells were telomerase positive (lane 1). Upon differentiation into specific lineages, telomerase activity diminished to undetectable levels (Lane 2). Lane 3 shows the positive control. Lane 4 represents negative control cell lysate, showing no telomerase activity. The telomeric length was evaluated by terminal restriction fragment (TRF) measurement (1G). C-kitpos cells had similar telomere lengths, both at early and late passages (250 PD) (lane 3 and 4, respectively) as compared with a high molecular weight marker, approximately 10.2 kbp (lane 2). Lane 1 represents a low molecular weight marker.
FIGS. 2A-2L demonstrate osteogenic induction of the c-kitpos cells isolated from chorionic villi and amniotic fluid. The shape of chorionic villi and amniotic c-kitpos cells ***treated*** with osteogenic-inducing medium after 4 days of induction changed to an osteoblast-like appearance (2A), whereas cells in the control medium did not lose their spindle-shaped phenotype (2B). Alkaline ***phosphatase*** activity was quantified in c-kitpos cells that were incubated with osteogenic-inducing and control medium for 32 days (2C). Numbers represent alkaline ***phosphatase*** production in nMol p-Nitrophenyl/min/106 cells, showing a peak of production at day 16 (solid line); whereas c-kitpos cells grown in control medium (shaded line) or c-kitpos cells grown in osteogenic conditions (dotted line) did not show any alkaline ***phosphatase*** production. C-kitpos cells ***treated*** with osteogenic-inducing medium and with control medium stained for alkaline ***phosphatase*** after 4, 8, 16, 24 and 32 days (2D). Strong alkaline ***phosphatase*** staining was noted in the osteogenic-induced cells starting at day 16, and remained high thereafter. C-kitpos cells grown in control medium did not show any alkaline ***phosphatase*** staining. When confluent, the cells formed typical lamellar structures similar to those found in bone (2F). C-kitpos cells in control medium did not form any lamellar structures (2E). Mineralization of cells was quantified using a chemical assay for calcium (2G). Numbers represent calcium deposition in mg/dl. Osteogenic-induced ckitpos cells showed a significant increase of calcium deposition starting at day 16 (solid line). No calcium deposition was detected in ckitpos cells grown in control medium (shaded line) or ckitpos cells grown in osteogenic conditions (dotted

line). Furthermore cells ***treated*** with control medium or with osteogenic-inducing medium were analyzed using von Kossa staining after 32 days in culture (40x). The osteogenic-induced cells showed significant mineralization starting at day 16 (2H). No mineralzation occurred at any time point in cells grown in control medium (2I). RNA was isolated from amniotic c-kitpos cells grown in control medium (lanes 1, 2, 3 and 4) and osteogenic-inducing medium (lanes 5, 6, 7 and 8) . RT-PCR was performed using primers for alkaline ***phosphatase*** , cbfa1, osteocalcin and beta 2-microglobulin at days 8, 16, 24 and 32 (2G). RT-PCR showed upregulation of cbfa1 and osteocalcin at day 8 and it confirmed the upregulation of alkaline ***phosphatase*** in the osteogenic-induced cells (2J). Ckitpos cells were seeded on hydroxyapatite-collagen scaffolds, induced into an osteogenic lineage, implanted subcutaneously in athymic mice, and harvested after 4 and 8 weeks. Bone-like tissue was evident, surrounded by an extracellular matrix. Toluidine blue staining confirmed the osteogenic phenotype. Large calcified areas within the implanted tissue stained positively with von Kossa, indicating bone formation (2K). Non seeded scaffold were implanted and used as control (2L).

FIGS. 3A-3F demonstrate adipogenic induction of the c-kitpos cells isolated from chorionic villi and amniotic fluid. Clusters of adipocytes appeared at 8 days (3A), and the percentage of cells increased with time until Oil-O-Red was uniformly staining the adipogenesis-induced cells at day 16 (3B). C-kitpos cells cultured in control medium did not show any ***lipid*** deposits at day 16 (3C). RNA was isolated from ckitpos cells grown in control (lanes 1 and 2) and adipogenicinducing (lanes 3 and 4) medium (3D). RT-PCR was performed using primers for PPAR gamma 2, lipoprotein lipase and P2microglobulin at days 8 and 16, as indicated. Upregulation of PPAR gamma 2 and lipoprotein lipase in cells grown in adipogenic-inducing medium was noted at days 8 and 16 (lanes 3 and 4). C-kitpos cells were seeded on polyglycolic acid polymer scaffolds. Cells were induced into an adipogenic lineage. The scaffolds were implanted subcutaneously in athymic mice, harvested after 4 and 8 weeks and analyzed. The retrieved scaffolds showed the formation of fatty tissues grossly (3E). The presence of adipose tissue was confirmed with Oil-O-Red staining (200x magnification) (3F).

FIGS. 4A-4I demonstrate myogenic induction of the c-kitpos cells isolated from chorionic villi and amniotic fluid. Under myogenic conditions the c-kitpos cells fused into multinucleated cells at day 4 (4A) and formed myotube-like structures after 8 days (4B). Multinucleated cells stained green for sarcomeric tropomyosin (4C) and desmin (4D) expression 16 days after myogenic induction. Cell nuclei were stained blue using DAPI. Untreated cells did not stain for sarcomeric tropomyosin (4E) or desmin (4F). RNA was isolated from c-kitpos cells grown in control (lanes 1 and 2) and myogenic-inducing (lanes 3 and 4) medium (4G). RT-PCR was performed using primers for MyoD, MRF4 (herculin, Myf6), and desmin at days 8 and 16. Myogenic-induced cells showed a strong upregulation of desmin expression at day 16 (lane 4). MyoD and MRF4 were induced with myogenic ***treatment*** at day 8 (lane 1). Specific PCR amplified DNA fragments of MyoD, MRF4 and Desmin could not be detected in the control cells at days 8 and 16 (lanes 1 and 2). C-kitpos cells were labeled with the fluorescence marker PKH26 and were induced into a myogenic lineage. The myogenic cells were injected into the hindlimb musculature of athymic mice and were retrieved after 4 weeks. The injected myogenic cells showed the formation of muscle tissue (m) which expressed desmin (4H) and maintained its fluorescence (4I). The native muscle (n) did not express any fluorescence.

FIGS. 5A-5F demonstrate endothelial induction of the c-kitpos cells isolated from chorionic villi and amniotic fluid. Ckitpos cells were cultured as monolayers in PBS-gelatin coated dishes with EBM-2 and bFGF and showed a typical endothelial appearance in vitro (5A). The fully differentiated endothelial cells stained for the endothelial specific markers FVIII (5B), KDR (5C) and P1H12 (5D). Once cultured in matrigel the cells were able to form capillary structures over time (5E). In order to confirm the phenotypic changes we performed RT-PCR 5(F). CD31 and VCAM showed a marked increased in the ckitpos cells induced in endothelial medium (lane 2). Ckitpos cells cultured in control medium (lane 1) did not show any ***gene*** amplification.

FIGS. 6A-6E demonstrate ***neurogenic*** induction of the c-kitpos cells isolated from chorionic villi and amniotic fluid. Ckitpos cells cultured under ***neurogenic*** inducing conditions changed their morphology within the first 24 hours. The cell cytoplasm retracted towards the nucleus, forming contracted multipolar structures, with primary and secondary branches, and cone-like terminal expansions (6A). The differentiated cells stained for specific ***neurogenic*** markers beta III Tubulin (6B), Nestin (6C), and

glial fibrillary acidic ***protein*** (GFAP) (6D). Only the Ckitpos cells cultured under ***neurogenic*** conditions showed the secretion of glutamic acid in the collected medium. Furthermore the secretion of glutamic acid could be induced (KCl; 20 min in 50 mM KCl buffer) (6E).

AB The present invention is directed to pluripotent fetal stem cells derived from chorionic villus, amniotic fluid, and placenta and the methods for isolating, expanding and differentiating these cells, and their therapeutic uses such as manipulating the fetal stem cells by gene transfection and other means for therapeutic applications.

CLMN 46 6 Figure(s).

FIGS. 1A-1G show results from chorionic villi and amniotic cell characterization experiments. Between 0.8 and 3% of the amniotic and chorionic villi cells were c-kitpos (1A). The ckitpos cells did not stain with mouse stage specific embryonic antigen 1 (1B), but stained positively for human stage specific embryonic antigens 3 and 4 (1C and 1D). Analyses of late passage c-kitpos cells (PD 200) showed a normal karyotype (1E). Telomerase activity was evaluated using the Telomerase Repeat Amplification Protocol (TRAP) assay (1F). The chorionic villi and amniotic c-kitpos cells were telomerase positive (lane 1). Upon differentiation into specific lineages, telomerase activity diminished to undetectable levels (Lane 2). Lane 3 shows the positive control. Lane 4 represents negative control cell lysate, showing no telomerase activity. The telomeric length was evaluated by terminal restriction fragment (TRF) measurement (1G). C-kitpos cells had similar telomere lengths, both at early and late passages (250 PD) (lane 3 and 4, respectively) as compared with a high molecular weight marker, approximately 10.2 kbp (lane 2). Lane 1 represents a low molecular weight marker.

FIGS. 2A-2L demonstrate osteogenic induction of the c-kitpos cells isolated from chorionic villi and amniotic fluid. The shape of chorionic villi and amniotic c-kitpos cells ***treated*** with osteogenic-inducing medium after 4 days of induction changed to an osteoblast-like appearance (2A), whereas cells in the control medium did not lose their spindle-shaped phenotype (2B). Alkaline ***phosphatase*** activity was quantified in c-kitpos cells that were incubated with osteogenic-inducing and control medium for 32 days (2C). Numbers represent alkaline ***phosphatase*** production in nMol p-Nitrophenyl/min/106 cells, showing a peak of production at day 16 (solid line); whereas c-kitpos cells grown in control medium (shaded line) or c-kitpos cells grown in osteogenic conditions (dotted line) did not show any alkaline ***phosphatase*** production. C-kitpos cells ***treated*** with osteogenic-inducing medium and with control medium stained for alkaline ***phosphatase*** after 4, 8, 16, 24 and 32 days (2D). Strong alkaline ***phosphatase*** staining was noted in the osteogenic-induced cells starting at day 16, and remained high thereafter. C-kitpos cells grown in control medium did not show any alkaline ***phosphatase*** staining. When confluent, the cells formed typical lamellar structures similar to those found in bone (2F). C-kitpos cells in control medium did not form any lamellar structures (2E). Mineralization of cells was quantified using a chemical assay for calcium (2G). Numbers represent calcium deposition in mg/dl. Osteogenic-induced ckitpos cells showed a significant increase of calcium deposition starting at day 16 (solid line). No calcium deposition was detected in ckitpos cells grown in control medium (shaded line) or ckitpos cells grown in osteogenic conditions (dotted line). Furthermore cells ***treated*** with control medium or with osteogenic-inducing medium were analyzed using von Kossa staining after 32 days in culture (40x). The osteogenic-induced cells showed significant mineralization starting at day 16 (2H). No mineralzation occurred at any time point in cells grown in control medium (2I). RNA was isolated from amniotic c-kitpos cells grown in control medium (lanes 1, 2, 3 and 4) and osteogenic-inducing medium (lanes 5, 6, 7 and 8) . RT-PCR was performed using primers for alkaline ***phosphatase*** , cbfa1, osteocalcin and beta 2-microglobulin at days 8, 16, 24 and 32 (2G). RT-PCR showed upregulation of cbfa1 and osteocalcin at day 8 and it confirmed the upregulation of alkaline ***phosphatase*** in the osteogenic-induced cells (2J). Ckitpos cells were seeded on hydroxyapatite-collagen scaffolds, induced into an osteogenic lineage, implanted subcutaneously in athymic mice, and harvested after 4 and 8 weeks. Bone-like tissue was evident, surrounded by an extracellular matrix. Toluidine blue staining confirmed the osteogenic phenotype. Large calcified areas within the

implanted tissue stained positively with von Kossa, indicating bone formation (2K). Non seeded scaffold were implanted and used as control (2L).

FIGS. 3A-3F demonstrate adipogenic induction of the c-kitpos cells isolated from chorionic villi and amniotic fluid. Clusters of adipocytes appeared at 8 days (3A), and the percentage of cells increased with time until Oil-O-Red was uniformly staining the adipogenesis-induced cells at day 16 (3B). C-kitpos cells cultured in control medium did not show any ***lipid*** deposits at day 16 (3C). RNA was isolated from ckitpos cells grown in control (lanes 1 and 2) and adipogenicinducing (lanes 3 and 4) medium (3D). RT-PCR was performed using primers for PPAR gamma 2, lipoprotein lipase and P2microglobulin at days 8 and 16, as indicated. Upregulation of PPAR gamma 2 and lipoprotein lipase in cells grown in adipogenic-inducing medium was noted at days 8 and 16 (lanes 3 and 4). C-kitpos cells were seeded on polyglycolic acid polymer scaffolds. Cells were induced into an adipogenic lineage. The scaffolds were implanted subcutaneously in athymic mice, harvested after 4 and 8 weeks and analyzed. The retrieved scaffolds showed the formation of fatty tissues grossly (3E). The presence of adipose tissue was confirmed with Oil-O-Red staining (200x magnification) (3F).

FIGS. 4A-4I demonstrate myogenic induction of the c-kitpos cells isolated from chorionic villi and amniotic fluid. Under myogenic conditions the c-kitpos cells fused into multinucleated cells at day 4 (4A) and formed myotube-like structures after 8 days (4B). Multinucleated cells stained green for sarcomeric tropomyosin (4C) and desmin (4D) expression 16 days after myogenic induction. Cell nuclei were stained blue using DAPI. Untreated cells did not stain for sarcomeric tropomyosin (4E) or desmin (4F). RNA was isolated from c-kitpos cells grown in control (lanes 1 and 2) and myogenic-inducing (lanes 3 and 4) medium (4G). RT-PCR was performed using primers for MyoD, MRF4 (herculin, Myf6), and desmin at days 8 and 16. Myogenic-induced cells showed a strong upregulation of desmin expression at day 16 (lane 4). MyoD and MRF4 were induced with myogenic ***treatment*** at day 8 (lane 1). Specific PCR amplified DNA fragments of MyoD, MRF4 and Desmin could not be detected in the control cells at days 8 and 16 (lanes 1 and 2). C-kitpos cells were labeled with the fluorescence marker PKH26 and were induced into a myogenic lineage. The myogenic cells were injected into the hindlimb musculature of athymic mice and were retrieved after 4 weeks. The injected myogenic cells showed the formation of muscle tissue (m) which expressed desmin (4H) and maintained its fluorescence (4I). The native muscle (n) did not express any fluorescence.

FIGS. 5A-5F demonstrate endothelial induction of the c-kitpos cells isolated from chorionic villi and amniotic fluid. Ckitpos cells were cultured as monolayers in PBS-gelatin coated dishes with EBM-2 and bFGF and showed a typical endothelial appearance in vitro (5A). The fully differentiated endothelial cells stained for the endothelial specific markers FVIII (5B), KDR (5C) and P1H12 (5D). Once cultured in matrigel the cells were able to form capillary structures over time (5E). In order to confirm the phenotypic changes we performed RT-PCR 5(F). CD31 and VCAM showed a marked increased in the ckitpos cells induced in endothelial medium (lane 2). Ckitpos cells cultured in control medium (lane 1) did not show any ***gene*** amplification.

FIGS. 6A-6E demonstrate ***neurogenic*** induction of the c-kitpos cells isolated from chorionic villi and amniotic fluid. Ckitpos cells cultured under ***neurogenic*** inducing conditions changed their morphology within the first 24 hours. The cell cytoplasm retracted towards the nucleus, forming contracted multipolar structures, with primary and secondary branches, and cone-like terminal expansions (6A). The differentiated cells stained for specific ***neurogenic*** markers beta III Tubulin (6B), Nestin (6C), and glial fibrillary acidic ***protein*** (GFAP) (6D). Only the Ckitpos cells cultured under ***neurogenic*** conditions showed the secretion of glutamic acid in the collected medium. Furthermore the secretion of glutamic acid could be induced (KCl; 20 min in 50 mM KCl buffer) (6E).

L12 ANSWER 9 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2004:63858 USPATFULL
TITLE: Methods for modulating splicing and/or alternative splicing, and for identifying alternatively spliced units in genes

INVENTOR(S): Chabot, Benoit, Sherbrooke, CANADA
Bolduc, Lucie, East Angus, CANADA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004048376	A1	20040311
APPLICATION INFO.:	US 2001-832183	A1	20010410 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	CA 2000-2305956	20000410

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: GOUDREAU GAGE DUBUC, 800 PLACE VICTORIA, SUITE 3400, MONTREAL, QUEBEC, H4Z 1E9
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 1460
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to splicing and especially to alternative RNA splicing which is involved in the production of protein isoforms with distinct activities. More specifically, the present invention relates to methods for modulating alternative splicing, and for identifying alternatively spliced units in genes. The present invention also concerns methods for modulating the ratio of alternatively spliced isoforms relative to each other and to normalize the alternative splicing actions of a splicing extract. The invention also relates to kits for normalizing and/or modulating splicing and/or alternative splicing of transcripts. More particularly the invention relates to a method to normalize a splicing and/or alternative splicing activity of an extract comprising an addition thereto of an effective amount of a polar aprotic solvent, whereby the effective amount normalizes splicing and/or alternative splicing as compared to an untreated extract. Examples of polar aprotic solvents of the invention include DMSO, DMF, formamide, HMPA, N-methylformamide, nitromethane, acetone, and acetonitrile.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 10 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2004:24683 USPATFULL
TITLE: Identification of dysregulated genes in patients with multiple sclerosis
INVENTOR(S): Dangond, Fernando, Newton, MA, UNITED STATES
Hwang, Daehee, Seattle, WA, UNITED STATES
PATENT ASSIGNEE(S): Brigham and Women's Hospital, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004018522	A1	20040129
APPLICATION INFO.:	US 2003-430762	A1	20030506 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-379284P	20020509 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FULBRIGHT & JAWORSKI L.L.P., Suite 2400, 600 CONGRESS AVENUE, AUSTIN, TX, 78701-3271
NUMBER OF CLAIMS: 46
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 7986
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention identifies a number of gene markers whose expression is altered in multiple sclerosis (MS). These markers can be used to diagnose or predict MS in subjects, and can be used in the monitoring of therapies. In addition, these genes identify therapeutic targets, the modification of which may prevent MS development or

progression.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 11 OF 20 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-625495 [60] WPIDS
DOC. NO. CPI: C2004-225008
TITLE: Decreasing infection of cell by virus, HIV, influenza A or Ebola, comprises interfering with activity or expression of host proteins or activity of host nucleic acids such as Rab9, AXL receptor tyrosine kinase, and Beta-chimerin .
DERWENT CLASS: B04 D16
INVENTOR(S): HODGE, T W; MOREY, N J; RUBIN, D; SANCHEZ, A; SHAW, M W; HODGE, T; MOREY, N; SHAW, M
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES; (UYVA-N) UNIV VANDERBILT; (USNA) US SEC OF NAVY
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004070002	A2	20040819	(200460)*	EN	396

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

AU 2003303308	A1	20040830	(200480)
EP 1613724	A2	20060111	(200604) EN

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004070002	A2	WO 2003-US37143	20031118
AU 2003303308	A1	AU 2003-303308	20031118
EP 1613724	A2	EP 2003-815298	20031118
		WO 2003-US37143	20031118

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003303308	A1 Based on	WO 2004070002
EP 1613724	A2 Based on	WO 2004070002

PRIORITY APPLN. INFO: US 2003-482604P 20030625; US 2002-427464P 20021118
AN 2004-625495 [60] WPIDS
AB WO2004070002 A UPAB: 20040920
NOVELTY - Decreasing infection of a host cell by a virus comprises interfering with an activity or expression of one or more host proteins or interfering with an activity of one or more host nucleic acids where the host protein or nucleic acid comprises Rab9, AXL receptor tyrosine kinase, Beta-chimerin and mammalian selenium binding protein.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) methods of decreasing HIV, Ebola, or influenza A infection of a host cell;
(2) a method of treating an HIV, Ebola, or influenza A viral infection in a host subject;
(3) a method of determining resistance or susceptibility to viral infection in a subject;
(4) a method of identifying a compound that decreases binding of a viral protein to a host protein and decreases viral infection;

(5) a method of decreasing infection of a host cell by a pathogen;

(6) a cell comprising a functional deletion of one or more target sequences associated with any of the 35 nucleotide sequences fully defined in the specification, where the cell has a decreased susceptibility to HIV infection;

(7) a cell comprising a functional deletion of one or more target sequences associated with any of the 27 nucleotide sequences fully defined in the specification, where the cell has a decreased susceptibility to influenza infection;

(8) a cell comprising a functional deletion of one or more target sequences associated with any of the 168 nucleotide sequences fully defined in the specification, where the cell has a decreased susceptibility to Ebola infection;

(9) a cell comprising a functional deletion of a Rab9 gene, where the cell has a decreased susceptibility to infection by a pathogen that uses lipid rafts; and

(10) a non-human transgenic mammal comprising any of the functional deletions cited above.

ACTIVITY - Virucide; Anti-HIV; Antibacterial.

MECHANISM OF ACTION - RNAi; RNA interference; Axl tryosine kinase receptor inhibitor; Rab9 inhibitor; beta chimerin inhibitor; retinoblastoma binding protein 1 inhibitor; protein cell control modulator; mammalian selenium binding protein inhibitor; KOX inhibitor.

Rab9, AXL (AXL receptor tyrosine kinase), CHN (Beta-chimerin), KOX, RBB (retinoblastoma binding protein 1), KIAA1259, F3 and mammalian selenium binding protein siRNA sequences were generated, pooled, hybridized to its appropriate complement sequence and used to transfect JC53 (HeLa cells modified to accept HIV), Vero (monkey kidney cells), MDCK (dog kidney cells, or HEK (human kidney cells). GFP siRNA sequences were used as negative controls.

Cells (20000 to 250000) were incubated in serum free media for 24 hours. Cocktails were made by mixing the siRNAs (50-100 pmoles) with lipofectamine 2000 (4-16 micro l) and RNAse inhibitor (1-4 micro l) in a solution of Optimem (serum free medium) in a total volume of 200-2000 micro l. Aliquots (50-500 micro l) of the cocktail were added to the cells which were incubated at 37 deg. C for 48 hours. The cells were then infected with HIV, Ebola, or influenza and the incubation continued for 3-7 days. Following transfection, several assays were conducted to confirm transfection efficiency and to determine the resistance of the cells to infection by various agents.

Quantitation of p24 levels of HIV infected J5C3 cells was determined. Rab9 siRNAs and mammalian selenium binding protein siRNAs each decreased HIV infection by 50% on day 4 post infection (day 7 post addition of siRNA). In addition, HIV infection decreased by 80-90% in the presence of beta-chimerin siRNAs, KOX siRNAs, or retinoblastoma binding protein 1 siRNA. However, HIV infection did not decrease in the presence of siRNAs that recognize KIAA1259, F3 or AXL siRNAs.

Infection of Ebola in HEK293 cells transfected with Rab9 or AXL siRNA was determined by measuring gp1 antigen using fluorescent antibody to gp1 envelope protein. Infection was decreased by 90-95% in presence of Rab9 siRNA, as compared to infection in absence of Rab9. Infection decreased by 80% in presence of AXL siRNA compared to absence.

USE - The method is useful for decreasing and treating infection of a host cell by a virus, such as HIV, influenza A or Ebola virus. Specifically, especially where the pathogen hijacks a lipid raft, the method is useful for decreasing infection of Campylobacter jejuni, Vibrio cholerae SV40, Legionella pneumophila, Aeromonas hydrophila, Echovirus l, Echovirus 11, Brucella spp., Clostridium spp., Avian sarcoma and leukosis virus, FimH, Escherichia coli, Streptococcus pyogenes, Semliki forest virus, Salmonella typhimurium, Bacillus anthracis, Ecotropic mouse leukaemia virus, Shigella flexneri, Bacillus thuringiensis, HTLV-I, Chlamydia spp., Helicobacter pylori, HFV-I, Mycobacterium spp., Listeria monocytogenes, Ebola, Marburg, Measles, Herpes Simplex virus, influenza virus, or Epstein-Barr virus (claimed).

Dwg.0/6

L12 ANSWER 12 OF 20 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-525062 [50] WPIDS
DOC. NO. NON-CPI: N2004-416127
DOC. NO. CPI: C2004-193206

TITLE: Evaluating the likelihood of an embryo to develop to term comprises removing a cell from an embryo; and evaluating the expression of at least two, and preferably at least three, preselected genes in the cell.
DERWENT CLASS: B04 D16 P31 P32 S03 S05
INVENTOR(S): POWERS, D; WANG, S
PATENT ASSIGNEE(S): (EMBR-N) EMBRYOMICS INC
COUNTRY COUNT: 29
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004055217	A1	20040701	(200450)*	EN	127
RW: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR					
W: AU CA US					
AU 2003293517	A1	20040709	(200474)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004055217	A1	WO 2003-US39450	20031212
AU 2003293517	A1	AU 2003-293517	20031212

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2003293517	A1	Based on	WO 2004055217

PRIORITY APPLN. INFO: US 2002-433426P 20021212
AN 2004-525062 [50] WPIDS
AB WO2004055217 A UPAB: 20040805
NOVELTY - Evaluating the likelihood of an embryo to develop to term comprises removing a cell from an embryo; and evaluating the expression of at least two, and preferably at least three, preselected genes in the cell, thus evaluating the embryo.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) a database, which comprises a plurality of records where each record includes at least one, two or preferably all of the following: data on the expression of at least two, preferably at least three genes obtained from a cell of an embryo; data on whether the embryo was carried to term; and data on a preselected factor present in one or both parents of the embryo;
(2) an array of a plurality of capture probes, where each of the capture probes is positionally distinguishable from other capture probes of the plurality on the array, where at least one probe, preferably at least two or three probes, hybridizes specifically with a gene the expression of which is predictive of the likelihood that an embryo which expresses the gene at a predetermined level will progress to term, and at least one probe which can specifically hybridize to a nucleic acid encoding or expressed by a specific allele of a selected gene such that it can distinguish between a first and second form of a gene;
(3) methods of providing information; and
(4) a method of evaluating a factor for its effect on the viability of an embryo.
USE - The method is useful for evaluating the likelihood of an embryo to develop to term (claimed).
Dwg.0/0

L12 ANSWER 13 OF 20 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-271642 [26] WPIDS
DOC. NO. NON-CPI: N2004-214925
DOC. NO. CPI: C2004-105604
TITLE: Novel isolated protein e.g., lipid phosphatase proteins encoded by plasticity-related genes useful for diagnosing and treating tumors such as neuroblastoma, astroglioma, ovarial cell carcinoma and breast cell carcinoma.

DERWENT CLASS: B04 D16 P14 S03
INVENTOR(S): BRAUER, A U; NINNEMANN, O; NITSCH, R; SAVASKAN, N E; BRAEUER, A U; SAVASKAN, N
PATENT ASSIGNEE(S): (UYBE-N) UNIV BERLIN CHARITE; (UYBE) UNIV BERLIN HUMBOLDT; (UYBE) CHARITE-UNIV MEDIZIN BERLIN
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1398372	A1	20040317 (200426)*		EN	66
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
WO 2004033691	A2	20040422 (200428)		EN	
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003298080	A1	20040504 (200465)			
EP 1537212	A2	20050608 (200537)		EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1398372	A1	EP 2003-2993	20030211
WO 2004033691	A2	WO 2003-EP10228	20030915
AU 2003298080	A1	AU 2003-298080	20030915
EP 1537212	A2	EP 2003-795778	20030915
		WO 2003-EP10228	20030915

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003298080	A1 Based on	WO 2004033691
EP 1537212	A2 Based on	WO 2004033691

PRIORITY APPLN. INFO: EP 2002-20679 20020913
AN 2004-271642 [26] WPIDS
AB EP 1398372 A UPAB: 20040421
NOVELTY - An isolated protein (I) e.g., lipid phosphatase protein comprising the same or substantially the same amino acid sequence chosen from a fully defined sequence (S1)-(S5) of 763, 746, 766, 716 and 766 amino acids as given in the specification, a splice variant or its salt, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a nucleic acid (II) which comprises at least one nucleic acid encoding (I);
(2) a nucleic acid (III) complementary to (II);
(3) a vector (IV) comprising (I), (II) and/or (III);
(4) an isolated cell (V) comprising (I), (II), (III) or (IV);
(5) a transgenic non-human animal (VI) generated from (V);
(6) an antibody (VII) directed against (I);
(7) producing (I), (II), or (III) involves cultivating (V) and isolating (I), (II) or (III); and
(8) a pharmaceutical composition (VIII) for the treatment of neuronal injuries or diseases, comprising (I), (II), (III), (IV), (VI), (VII), a binding compound isolated by using (I), (II) or (III) and/or a functional interactor isolated by using (I), (II) or (III) and if needed suitable auxiliary substances and/or additives.
ACTIVITY - Nootropic; Neuroprotective; Cerebroprotective.
No biological data given.
MECHANISM OF ACTION - None given.
USE - (I) is useful for isolating compounds interacting with (I)

which involves contacting (I) with at least one potentially interacting compound and measuring binding of the compound to (I). The above method further involves selecting a binding compound, modifying the binding compound, to generate a variety of modified binding compounds, contacting the protein with each of the modified binding compounds, measuring binding of the modified compounds to the protein, and if needed repeating the above steps for one or more times. (II) or (V) is useful for isolating functional interactors which involves contacting (V) e.g., neuronal cell that comprises (II) encoding (I), its splice variant or its fragment with a potential functional interactor, contacting (V) with a bioactive lipid phosphate, and measuring neurite movement.

The above method further involves:

(a) contacting (V) that comprises a mutant nucleic acid coding for a mutant of (I), or its splice variant or that contains a knock-out of the nucleic acid coding for one of the proteins with a potential functional interactor, contacting the cell with a bioactive lipid phosphate, and measuring neurite movement;

(b) the selecting a functional interactor, modifying the functional interactor to generate a variety of modified functional interactors, contacting (V) e.g., neuronal cell with each of the modified functional interactors, contacting (V) with a bioactive lipid phosphate, measuring neurite movement and if needed repeating the above steps for one or more times; and

(c) admixing the interacting compound or the functional interactor with suitable auxiliary substances and/or additives.

(I), (II) or (III) is useful as a diagnostic marker to the diagnosis of a disease or disease state, where the disease is a neuronal disease, a tumor disease or infertility. (VIII) is useful for producing medicament for the treatment of neuronal diseases or injuries (all claimed). (I) is useful for diagnosing and treating of tumors e.g., neuroblastoma, astroglioma, ovarial cell carcinoma, prostatic cell carcinoma and breast cell carcinoma. (VIII) is useful for treating neuronal injuries or diseases e.g., spinal cord lesion, Alzheimer's disease and stroke

Dwg.0/14

L12 ANSWER 14 OF 20 USPATFULL on STN DUPLICATE 1
ACCESSION NUMBER: 2003:133458 USPATFULL
TITLE: Therapeutic cell preparation grafts and methods of use thereof
INVENTOR(S): Klein, Matthew B., Los Altos, CA, UNITED STATES
Cuono, Charles B., Chandler, AZ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003091543	A1	20030515
APPLICATION INFO.:	US 2002-44004	A1	20020111 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-24057001	20011026

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MINTZ LEVIN COHN FERRIS GLOVSKY & POPEO, 666 THIRD AVENUE, NEW YORK, NY, 10017
NUMBER OF CLAIMS: 54
EXEMPLARY CLAIM: 1
LINE COUNT: 1636
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A biological preparation including genetically modified cells together with biocompatible matrices and methods of use thereof are provided. The biological preparation is useful in treating a subject at risk for or suffering from a disease in a controllable dosage and time-dependent manner, and for in vitro and in vivo screening of candidate drug therapies

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 15 OF 20 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-221609 [21] WPIDS
DOC. NO. CPI: C2003-056380

TITLE: Identifying an ABCA1 modulating agent for treating or reducing the risk of an ABCA1-related diseases e.g., Alzheimer's disease by contacting a compound with an ABCA1 dephosphorylating or phosphorylating enzyme.
DERWENT CLASS: B04 D16
INVENTOR(S): HAYDEN, M R; SEE, R
PATENT ASSIGNEE(S): (UYBR-N) UNIV BRITISH COLUMBIA; (XENO-N) XENON GENETICS INC
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003004692	A2	20030116 (200321)*		EN	54

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

AU 2002317093 A1 20030121 (200452)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003004692	A2	WO 2002-CA1001	20020703
AU 2002317093	A1	AU 2002-317093	20020703

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002317093	A1	Based on	WO 2003004692

PRIORITY APPLN. INFO: WO 2002-CA1085 20020702; US 2001-302854P 20010703
AN 2003-221609 [21] WPIDS
AB WO2003004692 A UPAB: 20030328
NOVELTY - Identifying an ABCA1 modulating agent comprises:
(a) contacting a compound with an ABCA1 dephosphorylating or phosphorylating enzyme in the presence of phosphorylated or unphosphorylated ABCA1 protein under conditions permitting dephosphorylation or phosphorylation, respectively; and
(b) determining a higher level of phosphorylated ABCA1 protein in the presence of the compound compared to when the compound is not present.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a method for producing a product;
(2) a method for treating or reducing the risk of an ABCA1-related disease;
(3) a method for modulating fertility; and
(4) a method for identifying an agent useful for modulating cholesterol levels.
ACTIVITY - Cardiant; Nootropic; Neuroprotective; Tranqulilizer; Vulnerary; Antiinfertility; Anti-cholesterol. No biological data given.
MECHANISM OF ACTION - ABCA1-Agonist.
USE - The method is useful for manufacturing a medicament for treating or reducing the risk of an ABCA1-related diseases such as cardiovascular disease or ABCA1-linked neurological disease, particularly Alzheimer's disease or a traumatic injury (claimed).
Dwg.0/13

L12 ANSWER 16 OF 20 IFIPAT COPYRIGHT 2006 IFI on STN
AN 10337738 IFIPAT;IFIUDB;IFICDB
TITLE: ADIPOSE-DERIVED STEM CELLS AND LATTICES; ANIMAL GROWTH REGULATORS; CONTROLLING CELL DIFFERENTIATION; TISSUE ENGINEERING
INVENTOR(S): Benhaim; Prosper, Encino, CA, US

Futrell; J. William, Pittsburgh, PA, US
Hedrick; Marc H., Encino, CA, US
Katz; Adam J., Charlottesville, VA, US
Llull; Ramon, Mallorca, ES
Lorenz; Hermann Peter, Belmont, CA, US
Zhu; Min, Los Angeles, CA, US
PATENT ASSIGNEE(S): Unassigned
PATENT ASSIGNEE PROBABLE: Unversity of (Probable)
AGENT: MANDEL & ADRIANO, 55 SOUTH LAKE AVENUE, SUITE 710, PASADENA, CA, 91101, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2003082152	A1	20030501
APPLICATION INFORMATION:	US 2001-952522		20010910

	APPLN. NUMBER	DATE	GRANTED PATENT NO. OR STATUS
CONTINUATION-IN-PART OF:	WO 2000-US6232	20000310	UNKNOWN

	NUMBER	DATE
PRIORITY APPLN. INFO.:	US 1999-123711P	19990310 (Provisional)
	US 1999-162462P	19991029 (Provisional)
FAMILY INFORMATION:	US 2003082152	20030501

DOCUMENT TYPE: Utility
Patent Application - First Publication
FILE SEGMENT: CHEMICAL
APPLICATION

PARENT CASE DATA:

This patent application is a continuation-in-part (CIP) of U.S. Ser. No. not yet known, filed Sep. 10, 2001, which corresponds to PCT application No. PCT/US00/06232, filed Mar. 10, 2000, which claims the benfit of the filing dates of U.S. Ser. No. 60/ 123,711, filed Mar. 10, 1999, and U.S. Ser. No. 60/162,462, filed Oct. 29, 1999. The contents of all of the foregoing application are incorporated by refernce in their entireties into the present patent application.

NUMBER OF CLAIMS: 43 43 Figure(s).
DESCRIPTION OF FIGURES:

FIG. 1. Morphology; growth kinetics and senescence of adiposederived stem cells over long-term culture. Panel A: The morphology of adipose-derived stem cells (e.g., a processed lipoaspirate or PLA) obtained from liposuctioned adipose tissue. Panel B: adipose-derived stem cells (PLAs) obtained from 3 donors, were cultured for an extended period and cumulative population doubling was measured and expressed as a function of passage number. Panel C: Senescence in adipose-derived stem cells (PLA) cultures as detected by staining for betagalactosidase expression at pH 6.0. Representative senescent cells are shown (arrows).

FIG. 2. Composition of the adipose-derived stem cells (PLA) as determined by indirect immunofluorescence (IF). Adipose-derived stem cells (PLA) and bone marrow stromal cells (BMS), were stained with the following antibodies: 1) anti-Factor VIII (FVIII); 2) anti-smooth muscle actin (SMA); and 3) ASO2 (ASO2). Factor VIII and smooth muscle actin expressing cells are shown (arrows).

FIG. 3. Composition of the adipose-derived stem cells (PLA) as determined by flow cytometry. Panel A: Flow cytometry of adipose-derived stem cells (PLA) samples using forward and side scatter (FS and SS, respectively). A representative adiposederived stem cells sample is shown. Panel B: The cell composition of a representative adipose-derived stem cells (PLA) sample from one donor was determined staining with the following monoclonal antibodies: anti-Factor VIII (FVIII), antismooth muscle actin (SMA), ASO2 and a monoclonal antibody to vimentin (VIM), an additional marker for cells of mesenchymal origin. Panel C: Flow cytometry data from 5 donors was collected and the mean number of positive events for each cellspecific marker is expressed as a percentage of total adiposederived stem cells (PLA) cell number.

FIG. 4. Adipose-derived stem cells (PLA) accumulate lipid-filled droplets upon

treatment with Adipogenic Medium (AM). Adiposederived stem cells (PLA), bone marrow-derived MSCs (MSC), and 3T3-L1 pre-adipocyte cells (3T3-L1) were cultured for two weeks in AM and stained with Oil Red O to identify lipid-filled intracellular vacuoles. Undifferentiated PLA cells maintained in Control Medium (-ve Control) were stained as a negative control.

FIG. 5. Adipose-derived stem cells (PLA) induced with Osteogenic Medium (OM) express Alkaline Phosphatase and are associated with a calcified extracellular matrix (ECM). Adipose-derived stem cells (PLA), bone marrow-derived MSCs (MSC) and a human osteoblast cell line (NHOst) were cultured in OM to induce osteogenesis. Cells were stained at 2 weeks for Alkaline Phosphatase activity (AP; red). The presence of a calcified extracellular matrix (black regions) was examined at 4 weeks (von Kossa). Undifferentiated adipose-derived stem cells maintained in Control Medium were examined for AP expression and matrix calcification as a negative control (-ve Control).

FIG. 6. Adipose-derived stem cells (PLA) treated with Chondrogenic Medium (CM) are associated with a proteoglycanrich matrix and express collagen type II. Adipose-derived stem cells (PLA) and MSCs (MSC) were cultured for 2 weeks in CM using the micromass technique to induce chondrogenesis. The cells were fixed and processed for the presence of sulfated proteoglycans with Alcian Blue under acidic conditions (Alcian Blue). Paraffin sections of human cartilage were used as a positive control (Cartilage) while undifferentiated PLAs maintained in Control Medium were processed as a negative control (-ve Control). In addition, the expression of cartilagespecific collagen type II (Collagen II) was examined in PLA cells and human cartilage sections. Adipose-derived stem cells cultured in Control Medium (-ve Control) were stained with Alcian Blue and for collagen II expression as a negative control.

FIG. 7. Adipose-derived stem cells (PLA) cultured in Myogenic Medium (MM) express the myosin heavy chain and MyoD1. Adiposederived stem cells (PLA) were treated with MM and stained with antibodies specific to skeletal muscle myosin heavy chain (Myosin) or MyoD1 (MyoD1). A human skeletal muscle cell line (SKM) was examined as a positive control. In addition, the presence of multinucleated cells in adipose-derived stem cells cultures is shown (PLA, inset box). Myosin and MyoD1 expression was also assessed in undifferentiated adipose-derived stem cells (-ve Control) as a negative control.

FIG. 8. Growth kinetics of adipose-derived stem cells (PLA). Panel A: adipose-derived stem cells, isolated from each donor, were seeded in triplicate at a density of 1 x 104 cells per well. Cell number was calculated after 24 hours (day 1) and every 48 hours subsequent to day 1 (days 3 through 11). Mean cell number for each donor was expressed with respect to culture time. The growth curves from 4 representative donors are shown (20 years-open squares, 39 years-open circles, 50 years-open triangles and 58 years-crosses). Results are expressed as mean+-SEM. Panel B: Population doubling was calculated in all donors from the log phase of each growth curve (i.e. from day 3 to day 9) and expressed according to age. The line of regression was calculated (n=20; r=0.62)

FIG. 9. Histological confirmation of adipogenic and osteogenic differentiation by adipose-derived stem cells (PLA). A: To confirm adipogenesis, cells were stained at 2 weeks postinduction with Oil Red O. Low and extensive adipogenic levels are shown (Panel 1-low; Panel 2-high). Adipose-derived stem cells cultured in non-inductive control medium were analyzed as negative controls (Panel 3). B: To quantify adipogenic differentiation, the number of Oil Red O-positive stained cells were counted within three defined regions. Two samples were analyzed from each donor. The mean number of Oil Red O-positive cells was determined and expressed as a percentage of total adipose-derived stem cells number as an indication of adipogenic differentiation. Differentiation was expressed with respect to age and the line of regression calculated (n=20; r=0. 016).

FIG. 10. Osteogenic differentiation decreases with increasing donor age. Panel A: To confirm osteogenesis, adipose-derived stem cells (PLA) were stained at 2 weeks post-induction for alkaline phosphotase (AP) activity (Panels 1 to 3) and at 4 weeks post-induction for matrix calcification using von Kossa staining (Panels 4 to 6). Osteogenic differentiation levels are shown (Panels 1/2-low; Panels 4/5-high). Adipose-derived stem cells cultured in non-inductive control medium were analyzed as negative controls (Panels 3 and 6). Panel B: To quantify osteogenic differentiation, the number of AP-positive stained cells were counted within three defined regions. Two samples were analyzed from each donor. The mean number of AP-positive cells was determined and expressed as a percentage of total adipose-derived stem cells number as an indication of the osteogenic differentiation. Differentiation was expressed with respect to age and the line of regression calculated (n=18; r=0.70). Panel C: Based on the

results of Panel B, the donor pool was divided into two age groups ((20 to 36 years (n=7) and 37 to 58 years (n=11)). The average level of osteogenic differentiation was calculated for each group and expressed as a percentage of total adipose-derived stem cells number. Statistical significance was determined using an unpaired student t test assuming unequal variances (p less-than 0.00 1). Differentiation is expressed as mean+-SEM.

FIG. 11. Osteoprogenitor cell number within an adipose-derived stem cell fraction (PLA fraction) does not significantly change with age. Osteoprogenitor cell number within the fraction was determined by identifying cells with osteogenic potential. Two groups of donors were examined (Group A=20 to 39 years (n=5), Group B=40-58 years (n=6)). Osteogenesis was confirmed by staining for AP activity. Colonies containing more than 10 APpositive cells (CFU/AP+) were counted and averaged as an indicator of the number of osteogenic precursors within each age group. Statistical significance was determined using an unpaired student t test assuming unequal variances (p=0.11). Values are expressed as mean CFU/AP++-SEM.

FIG. 12. Human adipose-derived stem cells (PLA) placed in micromass cultures and induced with chondrogenic media undergo cellular condensation and nodule formation. Adipose-derived stem cells induced under micromass conditions were stained with Alcian blue staining at pH 1 to detect the presence of sulfated proteoglycans. Panel A: cellular condensation; (Panel B) ridge formation; (Panel C) formation of three-dimensional spheroids are shown (magnification 100 x); (Panel D) negative control (control medium).

FIG. 13. Hematoxylin & Eosin, Goldner's trichrome, and Alcian blue staining of nodule paraffin sections from adipose-derived stem cells (PLA). Micromass cultures adipose-derived stem cells were treated with chondrogenic medium to form nodules, the nodules were embedded in paraffin and sectioned. Nodule sections were stained using conventional hematoxylin and eosin (Panels A and B) and a Goldner's trichrome stain to detect collagens (green) (Panels C and D). Adipose-derived stem cells induced for 2 days are shown at a magnification of 200 x (Panels A and C) and 14 days are shown at 100 x (Panels B and D) . In addition, sections were stained with Alcian blue staining at pH 1, to detect highly sulfated proteoglycans. Day two nodules (Panel E) are shown at a magnification of 200 x and day fourteen nodules (Panel F) are shown at 100 x .

DESCRIPTION OF FIGURES:

FIG. 14. Nodule differentiated from adipose-derived stem cells (PLA) express chondroitin-4-sulfate and keratin sulfate as well as cartilage-specific collagen type II. Nodules induced from adipose-derived stem cells for 2 days (Panels A and C) and 14 days (Panels B and D) were embedded in paraffin and sectioned. Sections were stained with monoclonal antibodies to the sulfated proteoglycans chondroitin-4-sulfate and keratin sulfate. Sections were also stained with monoclonal antibodies to collagen type II (Panels E and F) (magnification 200 x).

FIG. 15. RT-PCR analysis of nodules induced from adipose-derived stem cells confirms the expression of collagens type II and type X as well as expression of cartilage-specific proteoglycan and aggrecan. Adipose-derived stem cells induced for 2, 7, and 14 days in chondrogenic medium and non-inductive control medium were analyzed by RT-PCR for the expression of collagen type I (CN I), type II (CN II), and type X (CN X) as well as cartilagespecific proteoglycan (PG), aggrecan (AG), and osteocalcin (OC).

FIG. 16. Adipose-derived stem cells induced in Myogenic Medium express MyoD1. Panels A to C: adipose-derived stem cells (PLA) were stained with an antibody to MyoD1 following 1 week (Panel A), 3 weeks (Panel B) and 6 weeks (Panel C) induction in MM. Expression of MyoD1 in the nucleus of positive staining PLA cells is shown (arrows, magnification 200 x). Panels D to F: PLA cells induced for 1 week (Panel D), 3 weeks (Panel E) and 6 weeks (Panel F) in non-inductive control medium (CM) were processed as above as a negative control (magnification 200 x).

FIG. 17. Adipose-derived stem cells induced in Myogenic Medium express skeletal muscle myosin heavy chain. Panels A to C: adipose-derived stem cells (PLA) cells were stained with an antibody to the myosin heavy chain (myosin) following 1 week (Panel A), 3 weeks (Panel B) and 6 weeks (Panel C) induction in MM. Myosin-positive staining PLA cells are shown (arrows, magnification 200 x). Panels D to F: adipose-derived stem cells (PLA) cells induced for 1 week (Panel D), 3 weeks (Panel E) and 6 weeks (Panel F) in non-inductive CM were processed as above as a negative control (magnification 200 x).

FIG. 18. Adipose-derived stem cells cultured in Myogenic Medium form multi-nucleated cells. Panel A: Phase contrast of adiposederived stem cells (PLA) at 3 weeks (1) and 6 weeks (2) postinduction with MM (magnification 400 x). Multi-nucleated cells are shown (arrows). Panel B: Immunostaining of

adipose-derived stem cells (PLA) cells at 6 weeks post-induction with an antibody to the myosin heavy chain. Myosin-expressing multinucleated cells are shown (arrows).

FIG. 19: RT-PCR analysis of adipose-derived stem cells induced in MM. RT-PCR was performed on adipose-derived stem cells induced for 1, 3 and 6 weeks in MM (PLA-MM) or in CM (PLA-CM), using primers to human MyoD1 and myosin. RT-PCR analysis of human foreskin fibroblast (HFF) cells induced in MM (HFF-MM) was also performed as a negative control. Duplicate reactions were performed using a primer set to beta-actin as an internal control. PCR products were resolved by agarose gel electrophoresis and equalized using beta-actin levels.

FIG. 20. The proportion of MyoD1-positive adipose-derived stem cells increases with induction time. Histogram showing the mean number of MyoD1-positive, adipose-derived stem cells (PLA) after a 1, 3 and 6 week induction in MM (% of total PLA cells+SEM-hatched bars). The mean number of MyoD1-positive cells observed after induction of adipose-derived stem cells with CM (black bars) and HFF cells in MM (open bars) was also measured. The values for each experiment are shown in table format below. A statistical comparison of MyoD1 values from 1 to 6 weeks using a one-way ANOVA was performed (asterisks; P less-than 0. 001, F=18.9). Furthermore, an ANOVA was performed comparing the experimental and control values for each time point. The pvalues are shown (p less-than 0.0001).

FIG. 21. A time-dependent increase in myosin expression is observed in induced adipose-derived stem cells. Histogram showing the mean number of myosin-positive adipose-derived stem cells (PLA) after a 1, 3 and 6 week induction in myosin medium (MM) (% of total PLA cells+-SEM-hatched bars). The mean number of myosin-positive cells observed after induction of adiposederived stem cells with control medium (CM) (black bars), and human foreskin fibroblast cells (HFF) in myosin medium (MM) (open bars) was also measured. The values for each experiment are shown in table format below. A statistical comparison of myosin values from 1 to 6 weeks using a one-way ANOVA was performed (asterisks; P less-than 0.0001, F=75.5). Furthermore, an ANOVA was performed comparing the experimental and control values for each time point. The p-values are shown (p less-than 0.0001).

FIG. 22. Long-term chrondrogenic potetial of adipose-derived stem cells. Adipose-derived stem cells, at passage 1 (panel A), 3 (panel B), and 15 (panel C), were induced under micromass conditions and stained with Alcian blue staining at pH 1 to detect the presence of sulfated proteoglycans.

FIG. 23. The adipose-derived stem cells (PLA) express a unique set of CD markers. PLA cell and MSCs from human bone marrow were processed for IF for the indicated CD antigens. Cells were co-stained with DAPI to visualize nuclei (blue) and the fluorescent images combined.

FIG. 24. CD marker profile of adipose-derived stem cells (PLA) and bone marrow MSCs using flow cytometry. Panel A: Adiposederived stem cells were analyzed by FC using forward and side scatter to assess cell size and granularity (FSC-H and SSC-H, respectively). MSCs were analyzed as a control. Panel B: PLA cells were fixed and incubated for the indicated CD markers using fluorochrome-conjugated primary antibodies. Stained PLA cells were subsequently analyzed by FC. MSCs and PLA cells stained with fluorochrome-conjugated non-specific IgG were examined as a positive and negative control, respectively. All results were corrected for senescence and represent a total of 105 events.

FIG. 25. Osteogenic adipose-derived stem cells (PLA) can be characterized by distinct proliferative, synthetic and mineralization phases. Adipose-derived stem cells were harvested and plated into 35 mm tissue culture dishes in two sets of four plates per differentiation period. All dishes were maintained in Control medium until approximately 50% confluence was reached. The cells were induced with Osteogenic medium (OM) and cell number was counted at the indicated days. Cell number was expressed as the number of adipose-derived stem cells (# cells (105)) and plotted versus differentiation time (Panel A). For each time period, one dish was stained for alkaline phosphatase (AP) activity and one dish was stained using a Von Kossa stain (VK) to detect calcium phosphate (Panel B).

FIG. 26. Dexamethasone and 1,25-dihydroxyvitamin D3 differentially affect PLA osteogenesis: AP enzyme and calcium phosphate quantitation. Triplicate samples of PLA cells, MSCs and NHOsts were induced for up to 6 weeks in OM, containing either 10-7 M Dexamethasone (OM/Dex) or 10-8 M 1,25dihydroxyvitamin D3 (OM/VD). Cells were assayed for AP activity, total calcium content and total protein. AP levels were expressed as nmol p-nitrophenol formed per minute per microgram protein (nmol p-nitrophenol/min/ug). Calcium levels were expressed as mM calcium per microgram protein (mM Ca2+/ug). Noninduced PLA cells (Control) were

analyzed as a negative control. Values were expressed as the mean+-SD.
FIG. 27. Osteo-induced PLA cells express several genes consistent with osteogenic differentiation: RT-PCR and Microarray analyses. Panel A: PLA cells were cultured in either OM/Dex, OM/VD or non-inductive Control medium (Control) for the indicated days. Total RNA was isolated, cDNA synthesized and PCR amplification performed for the indicated genes. MSCs were induced in OM/Dex or OM/VD and NHOsts were induced for 2 and 3 weeks in OM/Dex as controls. Duplicate reactions were amplified using primers to beta-actin as an internal control. Panel B: PLA cells were induced for 3 weeks in OM/Dex or maintained in non-inductive control medium. Total RNA was isolated and subject to microarray analysis using a customized array containing the genes, OC, OP, ON, CBFA1, CNI and BSP.
FIG. 28. Osteo-induced PLA cells express several proteins consistent with osteogenic differentiation: Immunofluorescent and Western analyses. Panel A: PLA cells and MSCs were induced in OM/Dex or maintained in non-inductive Control medium (Control) for 21 days. Cells were processed for IF for the expression of OC, OP and ON. Cells were co-stained with DAPI to visualize nuclei (blue) and the fluorescent images combined. Panel B: PLA cells were cultured in OM/Dex or non-inductive Control medium (Control) for 7 and 21 days. Cell lysates were separated by electrophoresis and analyzed by Western blotting using antibodies to OP (alpha OP), ON (alpha ON), Decorin (alpha DEC), Biglycan (alpha BG) and CNI (alpha CNI). The expression of the transferrin receptor (alpha TfR) was used as an internal control.
FIG. 29. Adipogenic differentiation by adipose-derived stem cells (PLA) is accompanied by growth arrest. Adipose-derived stem cells were harvested and plated into 35 mm tissue culture dishes in one set of four plates per differentiation period. All dishes were maintained in Control medium until approximately 80% confluence was reached. The cells were induced with Adipogenic medium (AM) and cell number was counted at the indicated days. Cell number was expressed as the number of PLA cells (# cells (105)) and plotted versus differentiation time (Panel A). For each time period, one dish was stained with Oil Red O to detect lipid accumulation (Panel B).

DESCRIPTION OF FIGURES:

FIG. 30. Adipogenic PLA cells express GPDH activity. Triplicate samples of PLA cells and 3T3-L1 cells were induced for up to 5 weeks in AM (PLA-AM, 3T3-AM, respectively). The cells were assayed for GPDH activity and total ***protein*** . GPDH levels were expressed as units GPDH per microgram ***protein*** (GPDH/ug). Noninduced PLA cells were analyzed as a negative control (PLAControl). Values were expressed as mean+-SD.
FIG. 31. Adipose-derived stem cells express several genes consistent with adipogenic differentiation: RT-PCR: Adiposederived stem cells were induced in AM (AM) or maintained in noninductive Control medium (Control) for the indicated days. Cells were analyzed by RT-PCR for the indicated genes. MSCs and 3T3-L1 cells were induced in AM as controls. Duplicate reactions were amplified using primers to beta-actin as an internal control.
FIG. 32. Adipose-derived stem cell induced toward the chondrogenic lineage are associated with the proteoglycans keratan and chondroitin sulfate: Immunohistochemistry and Dimethyldimethylene blue assay. Panel A: Adipose-derived stem cells (PLA), under micromass conditions, were induced in chondrogenic medium (CM) or maintained in non-inductive Control medium (Control) for 7 days. Nodules were fixed, embedded in paraffin, sectioned and stained with Alcian Blue to identify sulfated proteoglycans. Sections were also stained for the expression of CNII, keratan sulfate (KS) and chondroitin-4sulfate (CS), followed by counter-staining using H&E. Panel B: Triplicate samples of PLA cells and NHCK cells were induced for up to 3 weeks in CM (PLA-CM, NHCK-CM, respectively). Proteoglycan levels (keratan sulfate and chondroitin sulfate) were determined and expressed as microgram proteoglycan per microgram total ***protein*** (ug PG/ug). Non-induced, Adiposederived stem cells (PLA-Control) were analyzed as a negative control. Values were expressed as the mean+-SD.
FIG. 33. Chondrogenic PLA cells express several genes consistent with cartilage differentiation: RT-PCR. PLA cells, under micromass culture conditions, were induced in CM for 4, 7, 10 and 14 days or maintained in non-inductive Control medium for 10 days (Control). Cells were analyzed by RT-PCR for the indicated genes. NHCK cells were induced in a commercial prochondrogenic medium as a positive control. Duplicate reactions were performed using primers to beta-actin as an internal control.
FIG. 34. PLA cells induced toward the myogenic lineage express several genes consistent with myogenic differentiation: RT-PCR analysis. PLA cells were induced in MM (PLA-MM) for 1, 3 and 6 weeks. Cells were analyzed by RT-PCR for

the expression of MyoD1 (MD1), myosin (MYS), myogenin (MG) and myf5 (MYF5). Total RNA prepared from human skeletal muscle (SKM) was analyzed as a positive control. Duplicate reactions were amplified using primers to beta-actin as an internal control.

FIG. 35. ADSCs express multiple markers consistent with multilineage capacity. ADSC Isolation: PLA cells were plated at extremely low confluency in order to result in isolated single cells. Cultures were maintained in Control medium until proliferation of single PLA cells resulted in the formation of well-defined colonies. The single PLA-cell derived colonies were termed Adipose Derived Stem Cells (ADSCs). ADSCs were harvested using sterile cloning rings and 0.25% trypsin/EDTA. The harvested ADSCs were amplified in Cloning Medium (15% FBS, 1% antibiotic/antimycotic in F12/DMEM (1:1)). Tri-lineage ADSC clones were differentiated in OM, AM and CM and multi-lineage capacity by IH using the following histological and IH assays: Alkaline ***Phosphatase*** (osteogenesis), Oil Red O (adipogenic) and Alcian Blue (chondrogenic).

FIG. 36. Isolation of multi-lineage clones from PLA populations does not alter the expression profile of CD markers. Dual- and tri-lineage clones were isolated and expanded from single PLA cells. The ***clone*** populations were processed for the expression of the indicated CD markers using IF. The ADSCs were co-stained with DAPI to visualize nuclei (blue) and the fluorescent images combined.

FIG. 37. ADSCs express multiple genes consistent with multilineage capacity. Tri-lineage ADSC clones were cultured in OM/ VD (ADSC-Bone), AM (ADSC-Fat) and CM (ADSC-Cartilage), in addition to control medium (ADSC-Control), followed by RT-PCR analysis for the indicated lineage-specific genes. beta-actin levels were analyzed as an internal control.

FIG. 38. PLA cells appear to exhibit ***neurogenic*** capacity in vitro. Panel A: Light micrographs of non-induced PLA cells (PLA0 hrs) and PLA cells induced with NM for 2 and 8 hrs (PLA-2hrs, PLA-8 hrs, respectively). Panel B: PLA cells were maintained in NM or Control medium for 5 hours (PLA-NM, PLA-Control, respectively) and analyzed by IH for expression of the following lineage-specific markers: NSE, trk-A, NeuN and MAP-2 (neural), GFAP (astrocytic). PC12 cells ***treated*** with NGF were also assessed as a positive control. Panel C: PLA cells were induced in NM for 4.5 and 9 hrs and analyzed by RT-PCR for the indicated genes. In addition, PLA cells were induced in NM for 9 hrs and maintained in NPMM for 1 week (NPMM). Non-induced PLA cells (Control) were analyzed as a negative control. PC12 cells were examined as a positive control, together with total RNA prepared from human brain (Brain).

FIG. 39. Clones isolated from adipose-derived stem cell fractions exhibit ***neurogenic*** potential. Clones were examined using imunnohistochemistry for adipogenic (oil red O stain), osteogenic (alkaline phosphotase), chondrogenic (Alcian blue stain), and ***neurogenic*** (anti-trka expression) differntiation.

FIG. 40. Osteogenic differentiation of the adipose-derived stem cells (PLA) does not significantly alter CD marker expression. PLA cells (Panel A) and MSCs (Panel B) were induced in OM for 3 weeks (PLA-Bone, MSC-Bone respectively), or maintained in noninductive Control medium (PLA-Control, MSC-Control). Cells were processed for IF for the expression of CD34, CD44, CD45 and CD90, co-stained with DAPI to visualize nuclei (blue) and the fluorescent images combined.

FIG. 41. Adipogenic differentiation results in subtle changes to the adipose-derived stem cells (PLA) CD marker profile. PLA cells (Panel A) and MSCs (Panel B) were induced in AM for 2 weeks (PLA-Fat, MSC-Fat, respectively) or maintained in noninductive Control medium (PLA-Control, MSC-Control). Cells were processed for IF for the expression of CD34, CD44, CD45 and CD90, co-stained with DAPI to visualize nuclei (blue) and the fluorescent images combined. To visualize adipocytes and their staining pattern, fluorescent images were combined with light micrographs (inset). ***Lipid*** -filled cells (white arrowsfluorescent image; black arrows-inset) and fibroblasts (filled white arrows-fluorescent image; filled black arrows-inset) are indicated.

FIG. 42. Differentiation alters the expression of specific CD markers on adipose-derived stem cells (PLA): Flow cytometry. Panel A: PLA cells were maintained for 2 weeks in Control medium (Control), or in OM (Osteogenic) or AM (Adipogenic). Cells were analyzed by FC using forward and side scatter to assess cell size and granularity (FSC-H and SSC-H, respectively) . Panels B and C: PLA cells were maintained for 2 weeks in Control medium (PLA-CM), or in OM (PLA-OM) or AM (PLA-AM). Cells were directly stained for the indicated CD markers using fluorochrome-conjugated primary antibodies and analyzed by FC. The adipose-derived stem cells, stained with fluorochromeconjugated

non-specific IgG, were examined as a negative control. All results were corrected for senescence and represent a total of 105 events.

FIG. 43. Differentiation of the adipose-derived stem cells (PLA) results in a change in ECM composition. PLA cells were induced for either 3 weeks in OM (PLA-Bone), 2 weeks in AM (PLA-Fat) or maintained in Control medium (PLA-Control). Cells were processed for IF using antibodies to collagen type I (CNI), type 4 (CNIV) and type 5 (CNV). Cells were co-stained with DAPI to visualize nuclei (blue) and the fluorescent images combined. Fluorescent images were combined with light micrographs (inset). ***Lipid*** -filled PLA cells (white arrows-fluorescent image; black arrows-inset) are indicated. Osteo-induced MSCs (MSC-Bone), adipo-induced MSCs (MSC-Fat) and non-induced MSCs (MSC-Control) were also analyzed. !

AB The present invention provides adipose-derived stem cells (ADSCs), adipose-derived stem cell-enriched fractions (ADSC-EF) and adipose-derivedlattices, alone and combined with the ADSCs of the invention. In one aspect, the present invention provides an ADSC substantially free of adipocytes and red blood cells and clonal populations of connective tissue stem cells. The ADSCs can be employed, alone or within biologically-compatible compositions, to generate differentiated tissues and structures, both in vivo and in vitro. Additionally, the ADSCs can be expanded and cultured to produce molecules such as hormones, and to provide conditioned culture media for supporting the growth and expansion of other cell populations. In another aspect, the present invention provides a adipose-derived lattice substantially devoid of cells, which includes extracellular matrix material from adipose tissue. The lattice can be used as a substrate to facilitate the growth and differentiation of cells, whether in vivo or in vitro, into anlagen or even mature tissues or structures.

CLMN 43 43 Figure(s).

FIG. 1. Morphology; growth kinetics and senescence of adiposederived stem cells over long-term culture. Panel A: The morphology of adipose-derived stem cells (e.g., a processed lipoaspirate or PLA) obtained from liposuctioned adipose tissue. Panel B: adipose-derived stem cells (PLAs) obtained from 3 donors, were cultured for an extended period and cumulative population doubling was measured and expressed as a function of passage number. Panel C: Senescence in adipose-derived stem cells (PLA) cultures as detected by staining for betagalactosidase expression at pH 6.0. Representative senescent cells are shown (arrows).

FIG. 2. Composition of the adipose-derived stem cells (PLA) as determined by indirect immunofluorescence (IF). Adipose-derived stem cells (PLA) and bone marrow stromal cells (BMS), were stained with the following antibodies: 1) anti-Factor VIII (FVIII); 2) anti-smooth muscle actin (SMA); and 3) ASO2 (ASO2). Factor VIII and smooth muscle actin expressing cells are shown (arrows).

FIG. 3. Composition of the adipose-derived stem cells (PLA) as determined by flow cytometry. Panel A: Flow cytometry of adipose-derived stem cells (PLA) samples using forward and side scatter (FS and SS, respectively). A representative adiposederived stem cells sample is shown. Panel B: The cell composition of a representative adipose-derived stem cells (PLA) sample from one donor was determined staining with the following monoclonal antibodies: anti-Factor VIII (FVIII), antismooth muscle actin (SMA), ASO2 and a monoclonal antibody to vimentin (VIM), an additional marker for cells of mesenchymal origin. Panel C: Flow cytometry data from 5 donors was collected and the mean number of positive events for each cellspecific marker is expressed as a percentage of total adiposederived stem cells (PLA) cell number.

FIG. 4. Adipose-derived stem cells (PLA) accumulate lipid-filled droplets upon treatment with Adipogenic Medium (AM). Adiposederived stem cells (PLA), bone marrow-derived MSCs (MSC), and 3T3-L1 pre-adipocyte cells (3T3-L1) were cultured for two weeks in AM and stained with Oil Red O to identify lipid-filled intracellular vacuoles. Undifferentiated PLA cells maintained in Control Medium (-ve Control) were stained as a negative control.

FIG. 5. Adipose-derived stem cells (PLA) induced with Osteogenic Medium (OM) express Alkaline Phosphatase and are associated with a calcified extracellular matrix (ECM). Adipose-derived stem cells (PLA), bone marrow-derived MSCs (MSC) and a human osteoblast cell line (NHOst) were cultured in OM to induce osteogenesis. Cells were stained at 2 weeks for Alkaline Phosphatase activity (AP; red). The presence of a calcified extracellular matrix (black regions) was examined at 4 weeks (von Kossa).

Undifferentiated adipose-derived stem cells maintained in Control Medium were examined for AP expression and matrix calcification as a negative control (-ve Control).

FIG. 6. Adipose-derived stem cells (PLA) treated with Chondrogenic Medium (CM) are associated with a proteoglycanrich matrix and express collagen type II. Adipose-derived stem cells (PLA) and MSCs (MSC) were cultured for 2 weeks in CM using the micromass technique to induce chondrogenesis. The cells were fixed and processed for the presence of sulfated proteoglycans with Alcian Blue under acidic conditions (Alcian Blue). Paraffin sections of human cartilage were used as a positive control (Cartilage) while undifferentiated PLAs maintained in Control Medium were processed as a negative control (-ve Control). In addition, the expression of cartilagespecific collagen type II (Collagen II) was examined in PLA cells and human cartilage sections. Adipose-derived stem cells cultured in Control Medium (-ve Control) were stained with Alcian Blue and for collagen II expression as a negative control.

FIG. 7. Adipose-derived stem cells (PLA) cultured in Myogenic Medium (MM) express the myosin heavy chain and MyoD1. Adiposederived stem cells (PLA) were treated with MM and stained with antibodies specific to skeletal muscle myosin heavy chain (Myosin) or MyoD1 (MyoD1). A human skeletal muscle cell line (SKM) was examined as a positive control. In addition, the presence of multinucleated cells in adipose-derived stem cells cultures is shown (PLA, inset box). Myosin and MyoD1 expression was also assessed in undifferentiated adipose-derived stem cells (-ve Control) as a negative control.

FIG. 8. Growth kinetics of adipose-derived stem cells (PLA). Panel A: adipose-derived stem cells, isolated from each donor, were seeded in triplicate at a density of 1 x 104 cells per well. Cell number was calculated after 24 hours (day 1) and every 48 hours subsequent to day 1 (days 3 through 11). Mean cell number for each donor was expressed with respect to culture time. The growth curves from 4 representative donors are shown (20 years-open squares, 39 years-open circles, 50 years-open triangles and 58 years-crosses). Results are expressed as mean+-SEM. Panel B: Population doubling was calculated in all donors from the log phase of each growth curve (i.e. from day 3 to day 9) and expressed according to age. The line of regression was calculated (n=20; r=0.62)

FIG. 9. Histological confirmation of adipogenic and osteogenic differentiation by adipose-derived stem cells (PLA). A: To confirm adipogenesis, cells were stained at 2 weeks postinduction with Oil Red O. Low and extensive adipogenic levels are shown (Panel 1-low; Panel 2-high). Adipose-derived stem cells cultured in non-inductive control medium were analyzed as negative controls (Panel 3). B: To quantify adipogenic differentiation, the number of Oil Red O-positive stained cells were counted within three defined regions. Two samples were analyzed from each donor. The mean number of Oil Red O-positive cells was determined and expressed as a percentage of total adipose-derived stem cells number as an indication of adipogenic differentiation. Differentiation was expressed with respect to age and the line of regression calculated (n=20; r=0. 016).

FIG. 10. Osteogenic differentiation decreases with increasing donor age. Panel A: To confirm osteogenesis, adipose-derived stem cells (PLA) were stained at 2 weeks post-induction for alkaline phosphotase (AP) activity (Panels 1 to 3) and at 4 weeks post-induction for matrix calcification using von Kossa staining (Panels 4 to 6). Osteogenic differentiation levels are shown (Panels 1/2-low; Panels 4/5-high). Adipose-derived stem cells cultured in non-inductive control medium were analyzed as negative controls (Panels 3 and 6). Panel B: To quantify osteogenic differentiation, the number of AP-positive stained cells were counted within three defined regions. Two samples were analyzed from each donor. The mean number of AP-positive cells was determined and expressed as a percentage of total adipose-derived stem cells number as an indication of the osteogenic differentiation. Differentiation was expressed with respect to age and the line of regression calculated (n=18; r=0.70). Panel C: Based on the results of Panel B, the donor pool was divided into two age groups ((20 to 36 years (n=7) and 37 to 58 years (n=11)). The average level of osteogenic differentiation was calculated for each group and expressed as a percentage of total adipose-derived stem cells number. Statistical significance was determined using an unpaired student t test assuming unequal variances (p less-than 0.00 1). Differentiation is expressed as mean+-SEM.

FIG. 11. Osteoprogenitor cell number within an adipose-derived stem cell fraction (PLA fraction) does not significantly change with age. Osteoprogenitor cell number within the fraction was determined by identifying cells with osteogenic potential. Two groups of donors were examined (Group A=20 to 39 years (n=5), Group B=40-58 years (n=6)). Osteogenesis was confirmed by staining for AP activity. Colonies containing more than 10 APpositive cells (CFU/AP+) were counted and averaged as an indicator of the number of osteogenic precursors within each age group. Statistical significance was determined using an unpaired student t test assuming unequal variances (p=0.11). Values are expressed as mean CFU/AP++-SEM.

FIG. 12. Human adipose-derived stem cells (PLA) placed in micromass cultures and induced with chondrogenic media undergo cellular condensation and nodule formation. Adipose-derived stem cells induced under micromass conditions were stained with Alcian blue staining at pH 1 to detect the presence of sulfated proteoglycans. Panel A: cellular condensation; (Panel B) ridge formation; (Panel C) formation of three-dimensional spheroids are shown (magnification 100 x); (Panel D) negative control (control medium).

FIG. 13. Hematoxylin & Eosin, Goldner's trichrome, and Alcian blue staining of nodule paraffin sections from adipose-derived stem cells (PLA). Micromass cultures adipose-derived stem cells were treated with chondrogenic medium to form nodules, the nodules were embedded in paraffin and sectioned. Nodule sections were stained using conventional hematoxylin and eosin (Panels A and B) and a Goldner's trichrome stain to detect collagens (green) (Panels C and D). Adipose-derived stem cells induced for 2 days are shown at a magnification of 200 x (Panels A and C) and 14 days are shown at 100 x (Panels B and D) . In addition, sections were stained with Alcian blue staining at pH 1, to detect highly sulfated proteoglycans. Day two nodules (Panel E) are shown at a magnification of 200 x and day fourteen nodules (Panel F) are shown at 100 x .

FIG. 14. Nodule differentiated from adipose-derived stem cells (PLA) express chondroitin-4-sulfate and keratin sulfate as well as cartilage-specific collagen type II. Nodules induced from adipose-derived stem cells for 2 days (Panels A and C) and 14 days (Panels B and D) were embedded in paraffin and sectioned. Sections were stained with monoclonal antibodies to the sulfated proteoglycans chondroitin-4-sulfate and keratin sulfate. Sections were also stained with monoclonal antibodies to collagen type II (Panels E and F) (magnification 200 x).

FIG. 15. RT-PCR analysis of nodules induced from adipose-derived stem cells confirms the expression of collagens type II and type X as well as expression of cartilage-specific proteoglycan and aggrecan. Adipose-derived stem cells induced for 2, 7, and 14 days in chondrogenic medium and non-inductive control medium were analyzed by RT-PCR for the expression of collagen type I (CN I), type II (CN II), and type X (CN X) as well as cartilagespecific proteoglycan (PG), aggrecan (AG), and osteocalcin (OC).

FIG. 16. Adipose-derived stem cells induced in Myogenic Medium express MyoD1. Panels A to C: adipose-derived stem cells (PLA) were stained with an antibody to MyoD1 following 1 week (Panel A), 3 weeks (Panel B) and 6 weeks (Panel C) induction in MM. Expression of MyoD1 in the nucleus of positive staining PLA cells is shown (arrows, magnification 200 x). Panels D to F: PLA cells induced for 1 week (Panel D), 3 weeks (Panel E) and 6 weeks (Panel F) in non-inductive control medium (CM) were processed as above as a negative control (magnification 200 x).

FIG. 17. Adipose-derived stem cells induced in Myogenic Medium express skeletal muscle myosin heavy chain. Panels A to C: adipose-derived stem cells (PLA) cells were stained with an antibody to the myosin heavy chain (myosin) following 1 week (Panel A), 3 weeks (Panel B) and 6 weeks (Panel C) induction in MM. Myosin-positive staining PLA cells are shown (arrows, magnification 200 x). Panels D to F: adipose-derived stem cells (PLA) cells induced for 1 week (Panel D), 3 weeks (Panel E) and 6 weeks (Panel F) in non-inductive CM were processed as above as a negative control (magnification 200 x).

FIG. 18. Adipose-derived stem cells cultured in Myogenic Medium form multi-nucleated cells. Panel A: Phase contrast of adiposederived stem cells (PLA) at 3 weeks (1) and 6 weeks (2) postinduction with MM (magnification 400 x). Multi-nucleated cells are shown (arrows). Panel B: Immunostaining of adipose-derived stem cells (PLA) cells at 6 weeks post-induction with an antibody to the myosin heavy chain.

Myosin-expressing multinucleated cells are shown (arrows).

FIG. 19: RT-PCR analysis of adipose-derived stem cells induced in MM. RT-PCR was performed on adipose-derived stem cells induced for 1, 3 and 6 weeks in MM (PLA-MM) or in CM (PLA-CM), using primers to human MyoD1 and myosin. RT-PCR analysis of human foreskin fibroblast (HFF) cells induced in MM (HFF-MM) was also performed as a negative control. Duplicate reactions were performed using a primer set to beta-actin as an internal control. PCR products were resolved by agarose gel electrophoresis and equalized using beta-actin levels.

FIG. 20. The proportion of MyoD1-positive adipose-derived stem cells increases with induction time. Histogram showing the mean number of MyoD1-positive, adipose-derived stem cells (PLA) after a 1, 3 and 6 week induction in MM (% of total PLA cells+SEM-hatched bars). The mean number of MyoD1-positive cells observed after induction of adipose-derived stem cells with CM (black bars) and HFF cells in MM (open bars) was also measured. The values for each experiment are shown in table format below. A statistical comparison of MyoD1 values from 1 to 6 weeks using a one-way ANOVA was performed (asterisks; P less-than 0. 001, F=18.9). Furthermore, an ANOVA was performed comparing the experimental and control values for each time point. The pvalues are shown (p less-than 0.0001).

FIG. 21. A time-dependent increase in myosin expression is observed in induced adipose-derived stem cells. Histogram showing the mean number of myosin-positive adipose-derived stem cells (PLA) after a 1, 3 and 6 week induction in myosin medium (MM) (% of total PLA cells+-SEM-hatched bars). The mean number of myosin-positive cells observed after induction of adiposederived stem cells with control medium (CM) (black bars), and human foreskin fibroblast cells (HFF) in myosin medium (MM) (open bars) was also measured. The values for each experiment are shown in table format below. A statistical comparison of myosin values from 1 to 6 weeks using a one-way ANOVA was performed (asterisks; P less-than 0.0001, F=75.5). Furthermore, an ANOVA was performed comparing the experimental and control values for each time point. The p-values are shown (p less-than 0.0001).

FIG. 22. Long-term chrondrogenic potetial of adipose-derived stem cells. Adipose-derived stem cells, at passage 1 (panel A), 3 (panel B), and 15 (panel C), were induced under micromass conditions and stained with Alcian blue staining at pH 1 to detect the presence of sulfated proteoglycans.

FIG. 23. The adipose-derived stem cells (PLA) express a unique set of CD markers. PLA cell and MSCs from human bone marrow were processed for IF for the indicated CD antigens. Cells were co-stained with DAPI to visualize nuclei (blue) and the fluorescent images combined.

FIG. 24. CD marker profile of adipose-derived stem cells (PLA) and bone marrow MSCs using flow cytometry. Panel A: Adiposederived stem cells were analyzed by FC using forward and side scatter to assess cell size and granularity (FSC-H and SSC-H, respectively). MSCs were analyzed as a control. Panel B: PLA cells were fixed and incubated for the indicated CD markers using fluorochrome-conjugated primary antibodies. Stained PLA cells were subsequently analyzed by FC. MSCs and PLA cells stained with fluorochrome-conjugated non-specific IgG were examined as a positive and negative control, respectively. All results were corrected for senescence and represent a total of 105 events.

FIG. 25. Osteogenic adipose-derived stem cells (PLA) can be characterized by distinct proliferative, synthetic and mineralization phases. Adipose-derived stem cells were harvested and plated into 35 mm tissue culture dishes in two sets of four plates per differentiation period. All dishes were maintained in Control medium until approximately 50% confluence was reached. The cells were induced with Osteogenic medium (OM) and cell number was counted at the indicated days. Cell number was expressed as the number of adipose-derived stem cells (# cells (105)) and plotted versus differentiation time (Panel A). For each time period, one dish was stained for alkaline phosphatase (AP) activity and one dish was stained using a Von Kossa stain (VK) to detect calcium phosphate (Panel B).

FIG. 26. Dexamethasone and 1,25-dihydroxyvitamin D3 differentially affect PLA osteogenesis: AP enzyme and calcium phosphate quantitation. Triplicate samples of PLA cells, MSCs and NHOsts were induced for up to 6 weeks in OM, containing either 10-7 M Dexamethasone (OM/Dex) or 10-8 M 1,25dihydroxyvitamin D3 (OM/VD). Cells were assayed for AP activity,

total calcium content and total protein. AP levels were expressed as nmol p-nitrophenol formed per minute per microgram protein (nmol p-nitrophenol/min/ug). Calcium levels were expressed as mM calcium per microgram protein (mM Ca2+/ug). Noninduced PLA cells (Control) were analyzed as a negative control. Values were expressed as the mean+-SD.

FIG. 27. Osteo-induced PLA cells express several genes consistent with osteogenic differentiation: RT-PCR and Microarray analyses. Panel A: PLA cells were cultured in either OM/Dex, OM/VD or non-inductive Control medium (Control) for the indicated days. Total RNA was isolated, cDNA synthesized and PCR amplification performed for the indicated genes. MSCs were induced in OM/Dex or OM/VD and NHOsts were induced for 2 and 3 weeks in OM/Dex as controls. Duplicate reactions were amplified using primers to beta-actin as an internal control. Panel B: PLA cells were induced for 3 weeks in OM/Dex or maintained in non-inductive control medium. Total RNA was isolated and subject to microarray analysis using a customized array containing the genes, OC, OP, ON, CBFA1, CNI and BSP.

FIG. 28. Osteo-induced PLA cells express several proteins consistent with osteogenic differentiation: Immunofluorescent and Western analyses. Panel A: PLA cells and MSCs were induced in OM/Dex or maintained in non-inductive Control medium (Control) for 21 days. Cells were processed for IF for the expression of OC, OP and ON. Cells were co-stained with DAPI to visualize nuclei (blue) and the fluorescent images combined. Panel B: PLA cells were cultured in OM/Dex or non-inductive Control medium (Control) for 7 and 21 days. Cell lysates were separated by electrophoresis and analyzed by Western blotting using antibodies to OP (alpha OP), ON (alpha ON), Decorin (alpha DEC), Biglycan (alpha BG) and CNI (alpha CNI). The expression of the transferrin receptor (alpha TfR) was used as an internal control.

FIG. 29. Adipogenic differentiation by adipose-derived stem cells (PLA) is accompanied by growth arrest. Adipose-derived stem cells were harvested and plated into 35 mm tissue culture dishes in one set of four plates per differentiation period. All dishes were maintained in Control medium until approximately 80% confluence was reached. The cells were induced with Adipogenic medium (AM) and cell number was counted at the indicated days. Cell number was expressed as the number of PLA cells (# cells (105)) and plotted versus differentiation time (Panel A). For each time period, one dish was stained with Oil Red O to detect lipid accumulation (Panel B).

FIG. 30. Adipogenic PLA cells express GPDH activity. Triplicate samples of PLA cells and 3T3-L1 cells were induced for up to 5 weeks in AM (PLA-AM, 3T3-AM, respectively). The cells were assayed for GPDH activity and total ***protein*** . GPDH levels were expressed as units GPDH per microgram ***protein*** (GPDH/ug). Noninduced PLA cells were analyzed as a negative control (PLAControl). Values were expressed as mean+-SD.

FIG. 31. Adipose-derived stem cells express several genes consistent with adipogenic differentiation: RT-PCR: Adiposederived stem cells were induced in AM (AM) or maintained in noninductive Control medium (Control) for the indicated days. Cells were analyzed by RT-PCR for the indicated genes. MSCs and 3T3-L1 cells were induced in AM as controls. Duplicate reactions were amplified using primers to beta-actin as an internal control.

FIG. 32. Adipose-derived stem cell induced toward the chondrogenic lineage are associated with the proteoglycans keratan and chondroitin sulfate: Immunohistochemistry and Dimethyldimethylene blue assay. Panel A: Adipose-derived stem cells (PLA), under micromass conditions, were induced in chondrogenic medium (CM) or maintained in non-inductive Control medium (Control) for 7 days. Nodules were fixed, embedded in paraffin, sectioned and stained with Alcian Blue to identify sulfated proteoglycans. Sections were also stained for the expression of CNII, keratan sulfate (KS) and chondroitin-4sulfate (CS), followed by counter-staining using H&E. Panel B: Triplicate samples of PLA cells and NHCK cells were induced for up to 3 weeks in CM (PLA-CM, NHCK-CM, respectively). Proteoglycan levels (keratan sulfate and chondroitin sulfate) were determined and expressed as microgram proteoglycan per microgram total ***protein*** (ug PG/ug). Non-induced, Adiposederived stem cells (PLA-Control) were analyzed as a negative control. Values were expressed as the mean+-SD.

FIG. 33. Chondrogenic PLA cells express several genes consistent with cartilage differentiation: RT-PCR. PLA cells, under micromass culture conditions, were induced in CM for 4, 7, 10 and 14 days or maintained in

non-inductive Control medium for 10 days (Control). Cells were analyzed by RT-PCR for the indicated genes. NHCK cells were induced in a commercial prochondrogenic medium as a positive control. Duplicate reactions were performed using primers to beta-actin as an internal control.

FIG. 34. PLA cells induced toward the myogenic lineage express several genes consistent with myogenic differentiation: RT-PCR analysis. PLA cells were induced in MM (PLA-MM) for 1, 3 and 6 weeks. Cells were analyzed by RT-PCR for the expression of MyoD1 (MD1), myosin (MYS), myogenin (MG) and myf5 (MYF5). Total RNA prepared from human skeletal muscle (SKM) was analyzed as a positive control. Duplicate reactions were amplified using primers to beta-actin as an internal control.

FIG. 35. ADSCs express multiple markers consistent with multilineage capacity. ADSC Isolation: PLA cells were plated at extremely low confluency in order to result in isolated single cells. Cultures were maintained in Control medium until proliferation of single PLA cells resulted in the formation of well-defined colonies. The single PLA-cell derived colonies were termed Adipose Derived Stem Cells (ADSCs). ADSCs were harvested using sterile cloning rings and 0.25% trypsin/EDTA. The harvested ADSCs were amplified in Cloning Medium (15% FBS, 1% antibiotic/antimycotic in F12/DMEM (1:1)). Tri-lineage ADSC clones were differentiated in OM, AM and CM and multi-lineage capacity by IH using the following histological and IH assays: Alkaline ***Phosphatase*** (osteogenesis), Oil Red O (adipogenic) and Alcian Blue (chondrogenic).

FIG. 36. Isolation of multi-lineage clones from PLA populations does not alter the expression profile of CD markers. Dual- and tri-lineage clones were isolated and expanded from single PLA cells. The ***clone*** populations were processed for the expression of the indicated CD markers using IF. The ADSCs were co-stained with DAPI to visualize nuclei (blue) and the fluorescent images combined.

FIG. 37. ADSCs express multiple genes consistent with multilineage capacity. Tri-lineage ADSC clones were cultured in OM/ VD (ADSC-Bone), AM (ADSC-Fat) and CM (ADSC-Cartilage), in addition to control medium (ADSC-Control), followed by RT-PCR analysis for the indicated lineage-specific genes. beta-actin levels were analyzed as an internal control.

FIG. 38. PLA cells appear to exhibit ***neurogenic*** capacity in vitro. Panel A: Light micrographs of non-induced PLA cells (PLA0 hrs) and PLA cells induced with NM for 2 and 8 hrs (PLA-2hrs, PLA-8 hrs, respectively). Panel B: PLA cells were maintained in NM or Control medium for 5 hours (PLA-NM, PLA-Control, respectively) and analyzed by IH for expression of the following lineage-specific markers: NSE, trk-A, NeuN and MAP-2 (neural), GFAP (astrocytic). PC12 cells ***treated*** with NGF were also assessed as a positive control. Panel C: PLA cells were induced in NM for 4.5 and 9 hrs and analyzed by RT-PCR for the indicated genes. In addition, PLA cells were induced in NM for 9 hrs and maintained in NPMM for 1 week (NPMM). Non-induced PLA cells (Control) were analyzed as a negative control. PC12 cells were examined as a positive control, together with total RNA prepared from human brain (Brain).

FIG. 39. Clones isolated from adipose-derived stem cell fractions exhibit ***neurogenic*** potential. Clones were examined using imunnohistochemistry for adipogenic (oil red O stain), osteogenic (alkaline phosphotase), chondrogenic (Alcian blue stain), and ***neurogenic*** (anti-trka expression) differntiation.

FIG. 40. Osteogenic differentiation of the adipose-derived stem cells (PLA) does not significantly alter CD marker expression. PLA cells (Panel A) and MSCs (Panel B) were induced in OM for 3 weeks (PLA-Bone, MSC-Bone respectively), or maintained in noninductive Control medium (PLA-Control, MSC-Control). Cells were processed for IF for the expression of CD34, CD44, CD45 and CD90, co-stained with DAPI to visualize nuclei (blue) and the fluorescent images combined.

FIG. 41. Adipogenic differentiation results in subtle changes to the adipose-derived stem cells (PLA) CD marker profile. PLA cells (Panel A) and MSCs (Panel B) were induced in AM for 2 weeks (PLA-Fat, MSC-Fat, respectively) or maintained in noninductive Control medium (PLA-Control, MSC-Control). Cells were processed for IF for the expression of CD34, CD44, CD45 and CD90, co-stained with DAPI to visualize nuclei (blue) and the fluorescent images combined. To visualize adipocytes and their staining pattern, fluorescent images were combined with light micrographs (inset). ***Lipid*** -filled cells (white arrowsfluorescent image;

black arrows-inset) and fibroblasts (filled white arrows-fluorescent image; filled black arrows-inset) are indicated.

FIG. 42. Differentiation alters the expression of specific CD markers on adipose-derived stem cells (PLA): Flow cytometry. Panel A: PLA cells were maintained for 2 weeks in Control medium (Control), or in OM (Osteogenic) or AM (Adipogenic). Cells were analyzed by FC using forward and side scatter to assess cell size and granularity (FSC-H and SSC-H, respectively). Panels B and C: PLA cells were maintained for 2 weeks in Control medium (PLA-CM), or in OM (PLA-OM) or AM (PLA-AM). Cells were directly stained for the indicated CD markers using fluorochrome-conjugated primary antibodies and analyzed by FC. The adipose-derived stem cells, stained with fluorochromeconjugated non-specific IgG, were examined as a negative control. All results were corrected for senescence and represent a total of 105 events.

FIG. 43. Differentiation of the adipose-derived stem cells (PLA) results in a change in ECM composition. PLA cells were induced for either 3 weeks in OM (PLA-Bone), 2 weeks in AM (PLA-Fat) or maintained in Control medium (PLA-Control). Cells were processed for IF using antibodies to collagen type 1 (CNI), type 4 (CNIV) and type 5 (CNV). Cells were co-stained with DAPI to visualize nuclei (blue) and the fluorescent images combined. Fluorescent images were combined with light micrographs (inset). ***Lipid*** -filled PLA cells (white arrows-fluorescent image; black arrows-inset) are indicated. Osteo-induced MSCs (MSC-Bone), adipo-induced MSCs (MSC-Fat) and non-induced MSCs (MSC-Control) were also analyzed. !

L12 ANSWER 17 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2002:12521 USPATFULL
TITLE: Combinations and methods for promoting in vivo liver cell proliferation and enhancing in vivo liver-directed gene transduction
INVENTOR(S): Alison, Malcolm R., London, UNITED KINGDOM
Coutelle, Charles, London, UNITED KINGDOM
Forbes, Stuart J., London, UNITED KINGDOM
Hodgson, Humphrey J.F., London, UNITED KINGDOM
Sarosi, Ildiko, Newbury Park, CA, UNITED STATES
Themis, Michael, Oxfordshire, UNITED KINGDOM
PATENT ASSIGNEE(S): Amgen, Inc., Thousand Oaks, CA, UNITED STATES, 91320 (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002006902	A1	20020117
	US 6790838	B2	20040914
APPLICATION INFO.:	US 2001-769204	A1	20010124 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1999-256630, filed on 23 Feb 1999, GRANTED, Pat. No. US 6248725
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LYON & LYON LLP, 633 WEST FIFTH STREET, SUITE 4700, LOS ANGELES, CA, 90071
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 986
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Combinations and methods for inducing a semi-synchronous wave of liver cell proliferation in vivo and combinations and methods for inducing a semi-synchronous wave of liver cell proliferation and achieving transduction of proliferating liver cells in vivo are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 18 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2002:291078 USPATFULL
TITLE: Polynucleotides and polypeptides derived from corn ear
INVENTOR(S): Lalgudi, Raghunath V., Clayton, MO, United States
Ito, Laura Y., Pleasanton, CA, United States
Sherman, Bradley K., Oakland, CA, United States
PATENT ASSIGNEE(S): Incyte Genomics, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6476212	B1	20021105
APPLICATION INFO.:	US 1999-313294		19990514 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-86722P	19980526 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Brusca, John S.
ASSISTANT EXAMINER: Moran, Marjorie A.
LEGAL REPRESENTATIVE: Incyte Genomics, Inc., Murry, Lynn E.
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 23084
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides purified, corn ear-derived polynucleotides (cdps) which encode corn ear-derived polypeptides (CDPs). The invention also provides for the use of cdps or their complements, oligonucleotides, or fragments in methods for determining altered gene expression, to recover regulatory elements, and to follow inheritance of desirable characteristics through hybrid breeding programs. The invention further provides for vectors and host cells containing cdps for the expression of CDPs. The invention additionally provides for (i) use of isolated and purified CDPs to induce antibodies and to screen libraries of compounds and (ii) use of anti-CDP antibodies in diagnostic assays.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 19 OF 20 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-619235 [66] WPIDS
DOC. NO. CPI: C2002-174989
TITLE: Altering gene expression in human embryonic stem cells for transplantation procedures and biomedical engineering, comprises introducing a polynucleotide containing a gene expression altering sequence into the population of cells.
DERWENT CLASS: B04 D16
INVENTOR(S): BENVENISTY, N; EIGES-AVNER, R; SCHULDINER, M; YANUKA, O
PATENT ASSIGNEE(S): (BENV-I) BENVENISTY N; (EIGE-I) EIGES-AVNER R; (SCHU-I) SCHULDINER M; (YANU-I) YANUKA O; (YISS) YISSUM RES DEV CO HEBREW UNIV JERUSALEM
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002061033	A2	20020808 (200266)*		EN	43

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZM ZW

US 2002127715 A1 20020912 (200267)
EP 1379624 A2 20040114 (200410) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
AU 2002247875 A1 20020812 (200427)
JP 2004520046 W 20040708 (200445) 75

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002061033	A2	WO 2001-IB2858	20011127

US 2002127715 A1 Provisional US 2000-253222P 20001127
Provisional US 2001-267664P 20010209
US 2001-995452 20011127
EP 1379624 A2 EP 2001-997000 20011127
WO 2001-IB2858 20011127
AU 2002247875 A1 AU 2002-247875 20011127
JP 2004520046 W WO 2001-IB2858 20011127
JP 2002-561590 20011127

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1379624	A2 Based on	WO 2002061033
AU 2002247875	A1 Based on	WO 2002061033
JP 2004520046	W Based on	WO 2002061033

PRIORITY APPLN. INFO: US 2001-267664P 20010209; US 2000-253222P 20001127; US 2001-995452 20011127

AN 2002-619235 [66] WPIDS

AB WO 200261033 A UPAB: 20021014

NOVELTY - Altering (M1) gene expression in a population of human embryonic stem cells (I) comprises introducing a polynucleotide containing a gene expression altering sequence into the population of cells, so that the gene expression in the embryonic stem cells prior to introducing the polynucleotide is measurably different from gene expression after introducing the polynucleotide.

DETAILED DESCRIPTION - Altering (M1) gene expression in a population of human embryonic stem cells (I) comprises introducing a polynucleotide containing a gene expression altering sequence into the population of cells, so that the gene expression in the embryonic stem cells prior to introducing the polynucleotide is measurably different from gene expression after introducing the polynucleotide. (M1) may also comprise introducing into the population of cells by electroporation or in the presence of a cationic polymer, a DNA sequence corresponding to an enhancer, a promoter, or a gene, so as to alter gene expression in the population of embryonic cells in an amount to permit cells containing the DNA sequence to be distinguished from cells without the DNA sequence.

INDEPENDENT CLAIMS are also included for

(1) purifying (M2) pluripotent (I) from heterogenous population of cells by:

(a) introducing into the cells DNA encoding a selectable marker under a promoter that is specifically active in undifferentiated cell;

(b) separating those cells expressing the marker from those not expressing the marker; and

(c) obtaining purified pluripotent cells;

(2) treating (M3) a human subject for a condition resulting from a deficiency of a selected cell type by:

(a) causing (I) to be transfected in vitro with a nucleic acid encoding a marker under a tissue-specific promoter;

(b) step (b) of (M1); and

(c) introducing the selected cell type into the subject to treat the condition;

(3) a cell population (II) with a substantially pure population of (I) containing an expression altering sequence of exogenous DNA;

(4) producing (M4) a clonal pluripotent cell population from a mixture of pluripotent and differentiated cells by:

(a) transfecting the mixture of cells in the presence of a cationic polymer or by electroporation with a DNA encoding a marker protein under a promoter that is selectively active in cells of the inner cell mass of the embryo; and

(b) separating (I) from the differentiated cells according to the presence or absence of an expressed marker to produce the clonal pluripotent cell population;

(5) regulating (M5) cell viability of a population of cells in a subject, where the cells are derived from a culture of (I) which has undergone directed differentiation by:

(a) introducing the cells into the subject, where the cells contain an exogenous DNA encoding a suicide gene, and are selected from

undifferentiated cells, partially differentiated or wholly differentiated cells; and

(b) treating the subject with an agent for activating a sequence of events leading to suicide in the cells in the subject in response to an adverse event associated with the introduced cells;

(6) screening (M6) an agent to determine an effect on differentiation of pluripotent cells in vitro by:

(a) adding the agent to an in vitro cell culture of a population of genetically engineered (I) expressing a detectable marker under a cell-specific promoter;

(b) providing the conditions for (I) to differentiate; and

(c) determining the effect of the agent on differentiation of pluripotent cells; and

(7) a reagent cell population (III) for supplying material for transplantation comprising pluripotent (I) modified by foreign genetic material which is DNA not normally present in (I); which occurs in embryonic stem cells but is not expressed in them at levels which are biologically significant; DNA which occurs in (I) and has been modified so that it is only expressed by selected derivative cells; or any DNA that can be modified to be expressed by embryonic cells, derivative cells alone or any of its combination.

ACTIVITY - Cytostatic; Anti-HIV; Neuroprotective; Antiarthritic; Dermatological; Antiparkinsonian; Nootropic; Nephrotropic; Hepatotropic; Vulnerary; Cardiant.

No suitable data given.

MECHANISM OF ACTION - Cell-Therapy.

USE - The methods are useful in transfecting human embryonic stem cells, forming clonal preparations of pluripotent stem cells, and enhancing a cell population in a human subject. The embryonic stem cells are useful as an unlimited source of cells for transplantation procedures, and as a component in biomedical engineering as well as providing clues on early stages of human development. The cells may also be used in treating cancer, immune disorders (e.g. AIDS), autoimmune diseases (e.g. multiple sclerosis, rheumatoid arthritis, scleroderma), diseases of aging, degenerative diseases, including neurodegenerative diseases (e.g Parkinson's or Alzheimer's disease), cardiomyopathies, liver or kidney diseases, and conditions associated with trauma.

Dwg.0/9

L12 ANSWER 20 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2001:93491 USPATFULL
TITLE: Combinations and methods for promoting in vivo liver cell proliferation and enhancing in vivo liver-directed gene transduction
INVENTOR(S): Alison, Malcom R., London, United Kingdom
Coutelle, Charles, London, United Kingdom
Forbes, Stuart J., Middlesex, United Kingdom
Hodgson, Humphrey J. F., London, United Kingdom
Sarosi, Ildiko, Thousand Oaks, CA, United States
Themis, Michael, Buckinghamshire, United Kingdom
PATENT ASSIGNEE(S): Amgen, Inc., Thousand Oaks, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6248725	B1	20010619
APPLICATION INFO.:	US 1999-256630		19990223 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Martin, Jill
LEGAL REPRESENTATIVE: Lyon & Lyon LLP
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1,11
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1186
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Combinations and methods for inducing a semi-synchronous wave of liver cell proliferation in vivo and combinations and methods for inducing a semi-synchronous wave of liver cell proliferation and achieving transduction of proliferating liver cells in vivo are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

L3 QUE ((PHOSPHATIDIC(S) ACID ADJ PHOSPHATASE) OR (ACID ADJ PHOSPH

FILE 'USPATFULL, EMBASE, MEDLINE, CAPLUS, ESBIOBASE, BIOSIS, BIOTECHNO, PASCAL, LIFESCI, SCISEARCH, TOXCENTER, CABA, WPIDS, IFIPAT, AGRICOLA'
ENTERED AT 11:40:54 ON 31 JAN 2006

L4 6170 S L3
L5 1171 S (GENE OR SEQUENCE OR POLYNUCLEOTIDE OR RECOMBINANT OR CLONE)(
L6 1171 S (PHOSPHATASE OR HYDROLASE)(S)L5
L7 1171 S PHOSPHATASE(S)L6
L8 21 S NEUTRO?(S)L7
L9 137 S NEURO?(S)L7
L10 21 S TREAT?(S)L9
L11 118 DUP REM L9 (19 DUPLICATES REMOVED)
L12 20 DUP REM L10 (1 DUPLICATE REMOVED)

=> log y